Asymmetric Total Synthesis of (+)-Danicalipin A

Takehiko Yoshimitsu,* Ryo Nakatani, Akihiro Kobayashi, Tetsuaki Tanaka

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan

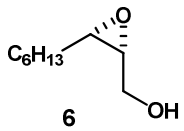
yoshimit@phs.osaka-u.ac.jp

Supporting Information

General Procedures S2
Epoxy alcohol **6** and Pivalate **7**: S2
Dichloride **8** and Dichloro alcohol **9**: S3
Determination of the relative configuration of dichloride **9**: S4
Dichloro alcohol *anti*-**10** and *syn*-**10**: S4
Determination of the relative configuration of *anti*-**10**: S5
Determination of the relative configuration of *syn*-**10**: S6
Enzymatic enantio-enrichment of *anti*-**10**: S6
Synthesis of C1-C11 fragment (Compound **5**): S7
Dichloro alcohol **13**: S7
Imine **12**: S8
Aldehyde **S4**: S8
TBS ether **14**: S8
Compound **15**: S9
Iodide **16**: S9
Nitro compound **5**: S10
Synthesis of C12-C22 gragment (Compound **4**): S10
Isoxazoline *anti*-**3** and *syn*-**3**: S11
Aldol **S5**: S12
Diol *anti*-**2** and *syn*-**2**: S13
Benzylidene acetal *anti*-**19**: S14
Determination of stereochemistry of compound **19** via Payne rearrangement: S15
TBS ether **17**: S18
Diol **18**: S19
(+)-Danicalipin A S20
Acetonide *anti*-**20**: S20
Acetonide *syn*-**21**: S21
^{1}H NMR/^{13}C NMR Spectra: S22
Comparison of ^{1}H NMR/^{13}C NMR Spectra of Synthetic and Natural Danicalipin A: S95-96
Determination of ees of epoxyalcohol **6** and vinyl alcohol **10** by Mosher Method S97-99
Determination of diastereoselectivity (ds) of compound **10**, **3**, and **2** by ^{1}H NMR analysis of the crude mixtures S100-102

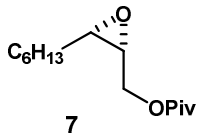
General: Melting points are uncorrected. All reagents were used as received from commercial suppliers unless otherwise noted. ^{1}H NMR spectra (500, 400 or 300 MHz) and ^{13}C NMR spectra (125, 100 or 75 MHz) were measured in the specified solvents. Chemical shifts are reported in ppm relative to the internal solvent signal [chloroform-*d*: 7.26 (^{1}H NMR), 77.0 (^{13}C NMR); methanol-d_4; 3.30 (^{1}H NMR), 49.0 (^{13}C NMR)]. The proton signal of TMS (0.00 ppm) was also used in some cases as the internal standard for ^{1}H NMR spectra. FT-IR spectra were recorded for samples loaded as neat films on NaCl plates. Mass spectra were obtained according to the specified technique. Analytical thin layer chromatography (TLC) was performed using Kieselgel60F_{254}, and compounds were visualized with UV light, anisaldehyde solution, phosphomolybdic acid in EtOH, iodine, or $KMnO_4$ solution.

Synthesis of epoxy alcohol 6:



6

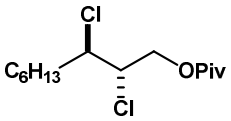
[(2*R*,3*S*)-3-Hexyloxiran-2-yl]methanol (**6**): To a magnetically stirred suspension of 4Å MS (3.2 g) in CH_2Cl_2 (180 mL) at -25 ^{o}C were added D-diethyl tartrate (0.86 mL, 5.06 mmol) and Ti(O*i*-Pr)$_4$ (0.93 mL, 3.17 mmol). After 1 h, TBHP (~5.5 M in decane with molecular sieve 4Å, 7.8 mL, 42.2 mmol) was added, and stirring was continued for an additional 35 min. To the mixture was added a solution of (*Z*)-non-2-en-1-ol (3.0 g, 21.1 mmol) in CH_2Cl_2 (30 mL), and the mixture was stirred at -25 ^{o}C for further 13 h. Following addition of brine and a 10% aqueous solution of NaOH, the mixture was allowed to warm to room temperature. After 30 min, Celite was added, and stirring was continued for further 3 h. The mixture was filtered through a Celite pad, and the filtrate was concentrated by rotary evaporation. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:4) to give epoxide **6** (3.12 g, 93%) as a colorless oil. The enantiomeric purity of this material was determined by Mosher method to be 80% ee. $[\alpha]^{26}_{D}$ +3.3 (*c* 0.66, $CHCl_3$, 80% ee) [lit.[1b] $[\alpha]^{25}_{D}$ +2.5 (*c* 2.2, $CHCl_3$, 90% ee)] All the spectroscopic data of this compound were in good agreement with those recorded in the literature. [1a,b]



7

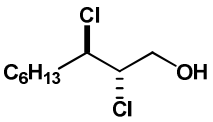
[(2*R*,3*S*)-3-Hexyloxiran-2-yl]methyl pivalate (**7**)**:** To a stirred solution of epoxide **6** (623 mg, 3.94 mmol) in CH_2Cl_2 (30 mL) at room temperature were added Et_3N (0.82 mL, 5.91 mmol), pivaloyl chloride (0.64 mL, 5.12 mmol), and DMAP (48.1 mg, 0.39 mmol). After 2.8 h, the mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. Purification of the residue

by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) gave epoxide **7** (905 mg, 95%) as a pale yellow oil. **Epoxide 7**: pale yellow oil; $[\alpha]^{21}_{D}$ +9.2 (*c* 1.38, $CHCl_3$, 80% ee); IR (neat) ν 2959, 2930, 1734, 1283, 1148 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.29 (dd, 1H, *J* = 12.1, 4.4 Hz), 4.05 (dd, 1H, *J* = 12.1, 6.8 Hz), 3.17 (ddd, 1H, *J* = 6.8, 4.4, 4.4 Hz), 3.01 (m, 1H), 1.59-1.25 (m, 10H), 1.23 (s, 9H), 0.89 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.4, 62.7, 56.4, 53.8, 38.7, 31.7, 29.0, 28.0, 27.1 (overlapped, 3 x C), 26.5, 22.5, 14.0; MS *m/z*: 243 $[M+H]^+$, 57 (100%); HRMS (FAB) calcd for $C_{14}H_{27}O_3$ $[M+H]^+$ 243.1960, found: 243.1976.



8

(2*S*,3*R*)-2,3-Dichlorononyl pivalate (**8**): To a stirred solution of epoxide **7** (891 mg, 3.68 mmol) in toluene (40 mL) at room temperature were added Ph_3P (2.89 g, 11.0 mmol) and NCS (1.47 g, 11.0 mmol). The mixture was heated at 90 ^oC for 1.5 h, and then an additional amount of NCS (0.49 g, 3.68 mmol) was added. After 1 h, the mixture was cooled with an ice bath and treated with sat. $NaHCO_3$ and TBHP (80% solution in di-*tert*-butylperoxide, 0.92 mL, 7.36 mmol). The mixture was poured into a separatory funnel where it was partitioned between EtOAc and sat. $Na_2S_2O_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (CH_2Cl_2/*n*-hexane 1:20) to give dichloride **8** (936 mg, 86%) as a colorless oil. **Dichloride 8**: colorless oil; $[\alpha]^{22}_{D}$ +8.4 (*c* 1.06, $CHCl_3$, 80% ee); IR (neat) ν 2959, 2930, 2861, 1738, 1479, 1460, 1283, 1152 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.50 (dd, 1H, *J* = 12.1, 3.8 Hz), 4.38 (dd, 1H, *J* = 12.1, 5.9 Hz), 4.16 (ddd, 1H, *J* = 7.5, 5.9, 3.8 Hz), 4.06 (ddd, 1H, *J* = 9.2, 7.5, 2.7 Hz), 2.02 (m, 1H), 1.78 (m, 1H), 1.57 (m, 1H), 1.50-1.15(m, 7H), 1.21 (s, 9H), 0.87 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 177.8, 65.1, 62.2, 61.6, 38.8, 34.6, 31.5, 28.5, 27.0 (overlapped, 3 x C), 25.6, 22.5, 14.0; MS *m/z*: 297 $[M+H]^+$, 57 (100%); HRMS (FAB) calcd for $C_{14}H_{27}O_2{}^{35}Cl_2$ $[M+H]^+$ 297.1388, found: 297.1407.

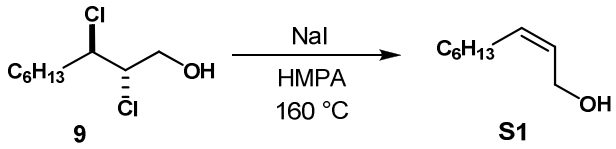


9

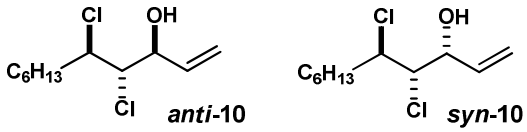
(2*S*,3*R*)-2,3-Dichlorononan-1-ol (**9**): To a stirred solution of dichloride **8** (907 mg, 3.05 mmol) in CH_2Cl_2 (30 mL) at -78^oC was added DIBAL (1.03 M in *n*-hexane, 6.8 mL, 7.02 mmol). After 20 min, sat. NH_4Cl was added, and the mixture was stirred at room temperature for 30 min. Celite was added to the solution, and the mixture was stirred for further 11 h and then filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) to give alcohol **9** (608 mg, 94%) as a colorless oil. **Alcohol 9**:

colorless oil; $[\alpha]^{23}_{D}$ +31.3 (*c* 1.03, $CHCl_3$, 80 % ee); IR (neat) ν 3366, 2955, 2928, 2859, 1458, 1067, 656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.15-4.00 (m, 4H), 2.06 (m, 1H), 1.98 (t, 1H, *J* = 6.9 Hz), 1.78 (m, 1H), 1.59 (m, 1H), 1.50-1.25 (m, 7H), 0.89 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 66.4, 64.5, 61.8, 34.9, 31.6, 28.6, 25.5, 22.5, 14.0; MS *m/z*: 146 $[M\text{-}CH_3OCl]^+$, 146 (100%); HRMS (EI) calcd for $C_8H_{15}{}^{35}Cl$ $[M\text{-}CH_3OCl]^+$ 146.0862, found: 146.0866.

Determination of the relative configuration of dichloride 9:



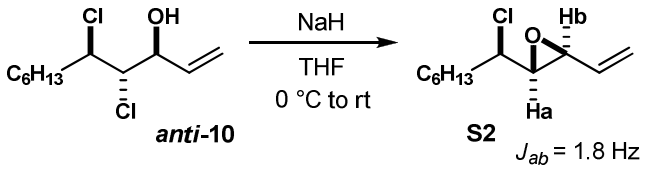
To a stirred solution of dichloride **9** (9.5 mg, 0.045 mmol) in HMPA (1.0 mL) at room temperature was added NaI (134 mg, 0.89 mmol). The mixture was heated at 160 °C for 1 h. After cooling, the mixture was poured into a separatory funnel where it was partitioned between Et_2O and sat. $Na_2S_2O_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:4) to give alcohol **S1** (6.7 mg, quant.) as a colorless oil. The material was identical in all respect with the authentic (*Z*)-allylic alcohol that was used as the starting material of the epoxidation reaction. The identity of alcohol **S1** obtained by the above-mentioned procedure was further confirmed by its transformation into *cis*-epoxide **6** with *m*CPBA.



(3*S*,4*S*,5*R*)-4,5-Dichloroundec-1-en-3-ol (*anti*-10), (3*R*,4*S*,5*R*)-4,5-Dichloroundec-1-en-3-ol (*syn*-10): To a stirred solution of alcohol **9** (520 mg, 2.44 mmol) in CH_2Cl_2 (24 mL) were added $NaHCO_3$ (1.02 g, 12.2 mmol) and Dess-Martin periodinane (1.45 g, 3.42 mmol) at room temperature. After 1 h, sat. $NaHCO_3$ and sat. $Na_2S_2O_3$ were added. The mixture was poured into a separatory funnel where it was extracted with Et_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue (567 mg) was dissolved in Et_2O (10 mL) and subjected to the next vinylation reaction without purification. The Et_2O solution of the crude aldehyde was added to a mixed solution of vinyl magnesiumbromide (1.0 M in THF, 7.32 mL, 7.32 mmol) and Et_2O (14 mL) at -78 °C, and the mixture was stirred for 1.3 h. Following addition of an additional amount of vinyl magnesiumbromide (1.0 M in THF, 2.44 mL, 2.44 mmol) at the same temperature, the mixture was stirred for further 40 min and then allowed to warm to 0 °C. After 1.5 h of stirring at the same temperature, the reaction was quenched with sat. NH_4Cl. The mitxture was poured into a separatory funnel where it was extracted with Et_2O. The organic phase was separated, dried over $MgSO_4$, filtered,

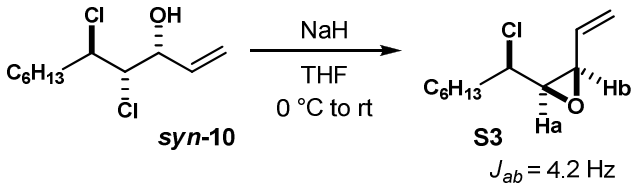
and concentrated. The residue was purified by flash silica gel column chromatography (toluene/*n*-hexane 1:1) to give less polar *syn*-alcohol **10** (147 mg, 25%) as a colorless oil and more polar *anti*-alcohol **10** (246 mg, 42%) as a colorless oil. ***Anti*-alcohol 10**: colorless oil; $[\alpha]^{24}_{D}$ +11.3 (*c* 0.45, $CHCl_3$, 80 % ee); IR (neat) ν 3383, 2957, 2926, 2859, 1466, 991, 934, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.93 (ddd, 1H, *J* = 17.4, 10.5, 6.9 Hz), 5.44 (d, 1H, *J* = 17.4 Hz), 5.36 (d, 1H, *J* = 10.5 Hz), 4.71 (m, 1H), 4.17 (dd, 1H, *J* = 9.2, 4.1 Hz), 3.94 (dt, 1H, *J* = 9.2, 2.3 Hz), 2.29 (d, 1H, *J* = 7.3 Hz), 2.09 (m, 1H), 1.79 (m, 1H), 1.58 (m, 1H), 1.48-1.20 (m, 7H), 0.90 (t, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.3, 119.4, 72.9, 69.1, 61.8, 34.4, 31.5, 28.6, 25.2, 22.5, 14.0; MS *m/z*: 203 $[M\text{-}Cl]^+$, 57 (100%); HRMS (EI) calcd for $C_{11}H_{20}O^{35}Cl$ $[M\text{-}Cl]^+$, 203.1203, found: 203.1204; *Anal*. Calcd for $C_{11}H_{20}OCl_2$ C 55.24, H 8.43, Cl 29.65, found: C 54.98, H 8.40, Cl 29.60. ***Syn*-alcohol 10**: colorless oil; $[\alpha]^{21}_{D}$ +49.3 (*c* 1.07, $CHCl_3$, 80 % ee); IR (neat) ν 3420, 2957, 2928, 2859, 990, 928, 656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.92 (ddd, 1H, *J* = 16.9, 10.5, 5.0 Hz), 5.39 (d, 1H, *J* = 16.9 Hz), 5.29 (d, 1H, *J* = 10.5 Hz), 4.84 (m, 1H), 4.22 (dt, 1H, *J* = 9.2, 2.3 Hz), 3.95 (dd, 1H, *J* = 9.2, 1.8 Hz), 2.12 (m, 1H), 2.09 (d, 1H, *J* = 9.2 Hz), 1.78 (m, 1H), 1.58 (m, 1H), 1.50-1.22 (m, 7H), 0.89 (t, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.5, 117.1, 71.4, 69.3, 61.7, 34.7, 31.6, 28.6, 25.2, 22.5, 14.0; MS *m/z*: 203 $[M\text{-}Cl]^+$, 57 (100%); HRMS (EI) calcd for $C_{11}H_{20}O^{35}Cl$ $[M\text{-}Cl]^+$, 203.1203, found: 203.1202; *Anal*. Calcd for $C_{11}H_{20}OCl_2$ C 55.24, H 8.43, Cl 29.65, found: C 55.02, H 8.36, Cl 29.41.

Determination of relative configuration of *anti*-alcohol 10:



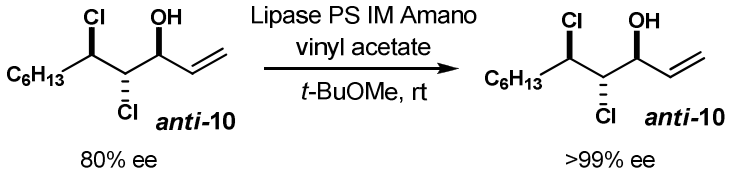
To a solution of *anti*-alcohol **10** (12.7 mg, 0.053 mmol) in THF (1.0 mL) at 0 °C was added NaH (60% in oil, 4.2 mg, 0.11 mmol). After being stirred at room temperature for 13 h, the mixture was poured into a separatory funnel where it was partitioned between sat. NH_4Cl and Et_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) to give epoxide **S2** (10.2 mg, 95 %) as a colorless oil. **Epoxide S2**: colorless oil; $[\alpha]^{20}_{D}$ -1.4 (*c* 0.51, $CHCl_3$, 80 % ee); IR (neat) ν 2955, 2926, 2855, 1732, 1456, 1260, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.59 (m, 1H), 5.50 (m, 1H), 5.32 (m, 1H), 3.65 (m, 1H), 3.34 (dd, 1H, *J* = 7.3, 1.8 Hz), 3.03 (dd, 1H, *J* = 7.3, 1.8 Hz), 1.89-1.74 (m, 2H), 1.60-1.18 (m, 8H), 0.94-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.2, 120.2, 62.9, 62.7, 58.9, 35.0, 31.6, 28.7, 26.2, 22.5, 14.0; MS *m/z*: 202 $[M]^+$, 69 (100%); HRMS (EI) calcd for $C_{11}H_{19}O^{35}Cl$ $[M]^+$ 202.1124, found: 202.1122.

Determination of relative configuration of *syn*-alcohol 10:



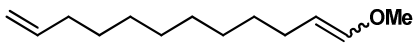
To a solution of *syn*-alcohol **10** (13.8 mg, 0.058 mmol) in THF (1.0 mL) at 0 ^{o}C was added NaH (60% in oil, 11.5 mg, 0.289 mmol). After being stirred at room temperature for 70 min, the mixture was poured into a separatory funnel where it was partitioned between sat. NH_4Cl and EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:50) to give epoxide **S3** (12 mg, quant.) as a colorless oil. **Epoxide S3**: colorless oil; $[\alpha]^{21}_{D}$ -19.9 (*c* 0.42, $CHCl_3$, 80% ee); IR (neat) ν 2955, 2926, 2855, 1460, 928 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.70 (ddd, 1H, *J* = 17.0, 10.3, 6.6 Hz), 5.53 (ddd, 1H, *J* = 17.0, 1.0, 1.0 Hz), 5.40 (ddd, 1H, *J* = 10.3, 1.0, 1.0 Hz), 3.67 (dt, 1H, *J* = 9.0, 5.5 Hz), 3.60 (ddd, 1H, *J* = 6.4, 4.2, 1.0 Hz), 3.21 (dd, 1H, *J* = 9.4, 4.2 Hz), 1.85-1.63 (m, 2H), 1.55-1.01 (m, 8H), 0.98-0.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 131.1, 121.3, 62.0, 60.9, 59.2, 34.9, 31.5, 28.7, 25.8, 22.5, 14.0; MS *m/z*: 203 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{11}H_{19}O^{35}Cl$ $[M+H]^+$ 203.1203, found: 203.1187.

Enzymatic enantio-enrichment of *anti*-alcohol 10:



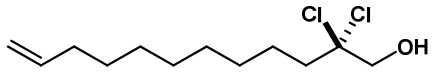
To a stirred solution of *anti*-alcohol **10** (239 mg, 1.00 mmol, 80% ee) in *t*-BuOMe (10 mL) at room temperature were added vinyl acetate (1.84 mL, 20.0 mmol), Lipase PS IM Amano (120 mg), and Et_3N (28 μL, 0.2 mmol). After being stirred at room temperature for 5 days, the mixture was filtered through a pad of Celite, and the filtrate was concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:40) to furnish *anti*-alcohol **10** (207 mg, 87%) as a colorless oil. $[\alpha]^{25}_{D}$ +13.6 (*c* 1.08, $CHCl_3$) (>99% ee); The enantiomeric purity of the material was determined by the Mosher method.

Synthesis of C1-C11 fragment 5:



11 (*E*:*Z* = 3:2)

1-Methoxydodeca-1,11-diene (11): To a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (18 g, 51.6 mmol) in THF (60 mL) at 0°C was added *t*-BuOK (5.06 g, 45.1 mmol). After 15 min, a solution of 10-undecenal (5.07 g, 30.1 mmol) in THF (40 mL) was added to the suspension, and the mixture was stirred for 20 min and then allowed to warm to room temperature. After 20 min, the mixture was cooled to 0°C, and TBHP (~5.5 M in decane with molecular sieve 4Å, 1.09 mL, 6.02 mmol) was added. After 10 min of stirring, the mixture was poured into a separatory funnel where it was partitioned between sat. $Na_2S_2O_3$ and EtOAc. The organic layer was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (*n*-hexane) to furnish diene **11** (4.91 g, 83 %) as a pale yellow oil. **Diene 11:** pale yellow oil; IR (neat) ν 2926, 2855, 1655, 1464, 1209, 1111, 934, 910 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.27* (d, 0.6H, *J* = 12.4 Hz), 5.88-5.76 (m, 1.4H, overlapped), 5.02-4.96 (m, 1H, overlapped), 4.95-4.90 (m, 1H, overlapped), 4.72* (dt, 0.6H, J=12.4, 7.3 Hz), 4.33 (dt, 0.4H, J=7.3, 6.4 Hz), 3.57 (s, 1.2H), 3.50* (s, 1.8H), 2.07-2.00 (m, 2.8H, overlapped), 1.94-1.87* (m, 1.2H), 1.42-1.25 (m, 12H, overlapped) (*The asterisk indicates the chemical shift of (*E*)-isomer **11**); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.9, 145.9, 139.1, 139. 0, 114.04, 114.01, 107.0, 103.0, 59.3, 55.6, 33.8, 30.8, 29.8, 29.5, 29.4, 29.2, 29.1, 29.0, 28.9, 27.7, 23.8; MS *m/z*: 196 $[M]^+$, 71 (100%); HRMS (EI) calcd for $C_{13}H_{24}O$ $[M]^+$ 196.1827, found: 196.1843.

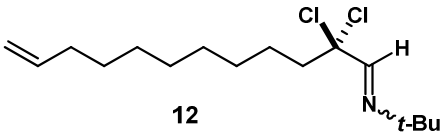


13

2,2-Dichlorododec-11-en-1-ol (13): To a solution of diene **11** (4.2 g, 21.4 mmol) in MeOH (200 mL) was added NCS (3.43 g, 25.7 mmol) at room temperature. After being stirred at the same temperature for 20 min, the mixture was concentrated under reduced pressure. The white residue was dissolved in 1,2-dichloroethane (200 mL), then TFA (4.12 mL, 53.5 mmol) was added to the solution at room temperature. After 42.5 h of stirring under reflux, the mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and water. The organic layer was separated, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The crude residue was used in the next step without further purification. The brown residue was dissolved in CH_2Cl_2 (200 mL) followed by the addition of *t*-$BuNH_2$ (2.72 mL, 25.7 mmol) and NCS (4.29 g, 32.1 mmol) at room temperature. After being stirred at the same temperature for 11.5 h, the mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. NH_4Cl. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was used in the next reaction without further purification. To a solution of the crude imine **12** (7.09 g) in CH_2Cl_2 (100 mL) was added 3 *N* HCl (100 mL) at room temperature. After stirring for 1 h, water was added, and the whole mixture was extracted with CH_2Cl_2. The organic extracts were combined, dried over $MgSO_4$,

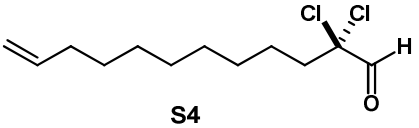
filtered, and concentrated. The crude aldehyde **S4** (6.13 g) thus obtained was dissolved in MeOH (200 mL), and the solution was cooled to 0 °C. To this was added $NaBH_4$ (972.5 mg, 25.7 mmol), and the mixture was stirred at room temperature for 50 min. Following evaporation of the solvent under reduced pressure, the residue was extracted with Et_2O and washed with sat. NH_4Cl. The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) to give alcohol **13** (3.44 g, 63%) as a pale yellow oil. **Alcohol 13**: pale yellow oil; IR (neat) ν 3383, 2926, 2855, 1640, 1456, 1071, 993, 910, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.80 (ddt, 1H, *J* = 16.9, 10.1, 6.9 Hz), 4.98 (d, 1H, *J* = 16.9 Hz), 4.92 (d, 1H, *J* = 10.1 Hz), 3.38 (d, 2H, *J* = 4.6 Hz), 2.66 (brs, 1H), 2.23-2.16 (m, 2H), 2.07-1.99 (m, 2H), 1.68-1.57 (m, 2H), 1.42-1.24 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.1, 114.1, 94.6, 72.0, 43.5, 33.7, 29.3, 29.00, 28.96, 28.8, 24.7; ^{13}C NMR (125 MHz, CD_3OD) δ: 140.1, 114.7, 95.6, 72.6, 44.6, 34.9, 30.5, 30.4, 30.2, 30.13, 30.07, 25.9; MS *m/z*: 252 $[M]^+$, 55 (100%); HRMS (EI) calcd for $C_{12}H_{22}O^{35}Cl_2$ $[M]^+$ 252.1048, found: 252.1051.

Provided below are the selected data of imine **12** and aldehyde **S4**.



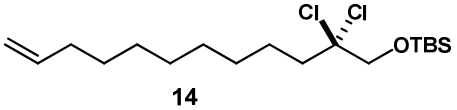
12

***N*-(2,2-Dichlorododec-11-enylidene)-2-methylpropan-2-amine (12)**: pale yellow oil, IR (neat) ν 2970, 2928, 2855, 1661, 1641, 1464, 1368, 1213, 991, 949, 910, 741, 673 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.56 (s, 1H), 5.75 (ddt, 1H, *J* = 16.9, 10.5, 6.9 Hz), 4.93 (m, 1H), 4.86 (m, 1H), 2.35-2.29 (m, 2H), 2.01-1.94 (m, 2H), 1.63-1.49 (m, 2H), 1.37-1.18 (m, 10H), 1.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.8, 139.1, 114.1, 90.5, 57.1, 43.4, 33.79, 33.75, 29.32, 29.30, 29.14 (overlapped, 3 x C), 29.05, 28.9, 25.0; MS *m/z*: 305 $[M]^+$, 209 (100%); HRMS (EI) calcd for $C_{16}H_{29}{}^{35}Cl_2N$ $[M]^+$ 305.1677, found: 305.1673.



S4

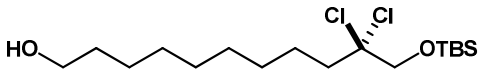
2,2-Dichlorododec-11-enal (S4): pale yellow oil, IR (neat) ν 2926, 2855, 1746, 1441, 1132, 991, 910, 723, 685, 667, 610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.25 (s, 1H), 5.81 (ddt, 1H, *J* = 16.9, 10.5, 6.9 Hz), 4.99 (ddt, 1H, *J* = 16.9, 2.3, 1.4 Hz), 4.93 (m, 1H), 2.30-2.23 (m, 2H), 2.08-2.00 (m, 2H), 1.67-1.57 (m, 2H), 1.44-1.24 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.0, 139.1, 114.2, 88.7, 40.5, 33.7, 29.23, 29.18, 28.99, 28.96, 28.8, 24.4.



14

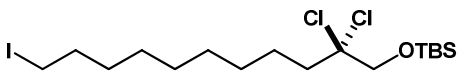
***tert*-Butyl(2,2-dichlorododec-11-enyloxy)dimethylsilane (14)**: To a stirred solution of alcohol **13** (3.08 g, 12.2 mmol) in CH_2Cl_2 (100 mL) at 0 °C were added 2,6-lutidine (2.8 mL, 24.4 mmol) and

TBSOTf (3.2 ml, 18.2 mmol). After 25 min, the mixture was poured into a separatory funnel where it was partitioned between sat. $NaHCO_3$ and CH_2Cl_2. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (*n*-hexane) to give TBS ether **14** (4.26 g, 95%) as a pale yellow oil. **TBS ether 14**: pale yellow oil; IR (neat) ν 2928, 2857, 1464, 1258, 1155, 1119, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.81 (ddt, 1H, *J* = 16.9, 10.1, 6.9 Hz), 4.99 (ddt, 1H, *J* = 16.9, 1.8, 1.8 Hz), 4.93 (m, 1H), 3.92 (s, 2H), 2.20-2.14 (m, 2H), 2.08-2.01 (m, 2H), 1.63-1.53 (m, 2H), 1.42-1.24 (m, 10H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.2, 114.1, 93.5, 72.1, 43.5, 33.8, 29.32, 29.30, 29.1, 29.0, 28.9, 25.7 (overlapped, 3 x C), 24.7, 18.3, -5.4 (overlapped, 2 x C); MS *m/z*: 367 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{18}H_{37}O^{35}Cl_2Si$ $[M+H]^+$ 367.1991, found: 367.1954.



15

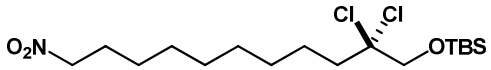
11-(*tert*-Butyldimethylsilyloxy)-10,10-dichloroundecan-1-ol (15): TBS ether **14** (2.2 g, 5.99 mmol) was dissolved in CH_2Cl_2 (60 mL), and the solution was cooled to -78 °C. An outlet stream containing O_3 and O_2 from an ozonizer was introduced into the mixture at -78 °C for 40 min. After being quenched with Ph_3P (1.88 g, 7.18 mmol), the mixture was allowed to warm to room temperature. After 4.5 h of strring, the mixture was concentrated under reduced pressure to give the crude aldehyde (4.3 g) as a colorless oil. The crude material was used in the next reaction without further purification. To a solution of aldehyde (4.3 g) in MeOH (60 mL) at 0 °C was added $NaBH_4$ (272 mg, 7.18 mmol). After being stirred at room temperature for 30 min, the mixture was concentrated under reduced pressure and poured into a separatory funnel where it was partitioned between Et_2O and sat. NH_4Cl. The organics were separated, filtered, dried over $MgSO_4$, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:5) to give alcohol **15** (1.86 g, 84%) as a colorless oil. **Alcohol 15**: colorless oil; IR (neat) ν 3335, 2886, 2857, 1464, 1258, 1153, 1119, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 3.92 (s, 2H), 3.64 (t, 2H, *J* = 6.9 Hz), 2.20-2.13 (m, 2H), 1.63-1.52 (m, 4H), 1.42-1.23 (m, 10H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 93.5, 72.1, 63.0, 43.5, 32.7, 29.4, 29.35, 29.29, 29.0, 25.71 (overlapped, 3 x C), 25.70, 24.7, 18.3, -5.4 (overlapped, 2 x C); MS *m/z*: 371 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{17}H_{37}O_2{}^{35}Cl_2Si$ $[M+H]^+$ 371.1940, found: 371.1941.



16

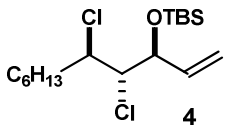
***tert*-Butyl(2,2-dichloro-11-iodoundecyloxy)dimethylsilane (16)**: To a stirred solution of alcohol **15** (3.75 g, 10.1 mmol) in THF (100 mL) were added imidazole (1.03 mg, 15.1 mmol), Ph_3P

(3.97 g, 15.1 mmol), and iodine (1.92 mg, 15.1 mmol) at room temperature. After 15 min, further amounts of imidazole (515 mg, 7.55 mmol), Ph_3P (1.99 mg, 7.55 mmol), and iodine (960 mg, 7.55 mmol) were added. After 15 min, sat. $NaHCO_3$ and TBHP (~5.5 M in decane with molecular sieve 4Å, 2.39 mL, 13.1 mmol) were added, and stirring was continued for further 10 min. The mixture was poured into a separatory funnel where it was partitioned between sat. $Na_2S_2O_3$ and Et_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (*n*-hexane) to give iodide **16** (4.75 g, 98%) as a colorless oil. **Iodide 16**: colorless oil; IR (neat) ν 2928, 2855, 1462, 1256, 1155, 1119, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 3.92 (s, 2H), 3.19 (t, 2H, *J* = 7.3 Hz), 2.20-2.14 (m, 2H), 1.87-1.78 (m, 2H), 1.63-1.54 (m, 2H), 1.44-1.24 (m, 10H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 93.4, 72.1, 43.4, 33.5, 30.4, 29.24, 29.21, 29.0, 28.5, 25.7 (overlapped, 3 x C), 24.7, 18.2, 7.3, -5.4 (overlapped, 2 x C); MS *m/z*: 481 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{17}H_{36}O^{35}Cl_2ISi$ $[M+H]^+$ 481.0958, found: 481.0944.



5

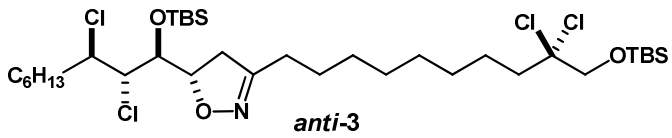
***tert*-Butyl(2,2-dichloro-11-nitroundecyloxy)dimethylsilane (5)**: To a stirred solution of iodide **16** (2.1 g, 4.36 mmol) in DMF (44 mL) at room temperature was added $NaNO_2$ (361 mg, 5.24 mmol). After 20 min, 20% aq. NaCl solution was added to the mixture, and the mixture was poured into a separatory funnel where it was extracted with Et_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) to give nitro compound **5** (1.04 g, 60%) as a colorless oil. In this process, nitrite ester was also produced as a byproduct which, by treatment with DIBAL, could be converted into the starting alcohol **15**. **Nitro compound 5**: colorless oil; IR (neat) ν 2928, 2857, 1555, 1258, 1152, 1119, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.38 (t, 2H, *J* = 6.9 Hz), 3.92 (s, 2H), 2.20-2.14 (m, 2H), 2.06-1.96 (m, 2H), 1.64-1.53 (m, 2H), 1.43-1.26 (m, 10H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 93.4, 75.7, 72.1, 43.4, 29.1, 29.0, 28.9, 28.7, 27.3, 26.2, 25.7 (overlapped, 3 x C), 24.7, 18.2, -5.4 (overlapped, 2 x C); MS *m/z*: 400; $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{17}H_{36}O_3N^{35}Cl_2Si$ $[M+H]^+$ 400.1842, found: 400.1829.



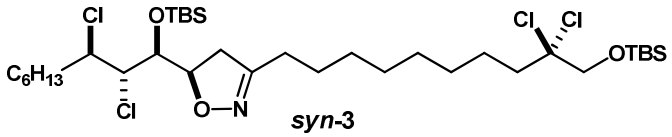
4

***tert*-Butyl((3*S*,4*S*,5*R*)-4,5-dichloroundec-1-en-3-yloxy)dimethylsilane (4)**: To a stirred solution of *anti*-alcohol **10** (335 mg, 1.40 mmol) in CH_2Cl_2 (14 mL) were added 2,6-lutidine (0.2 mL, 1.72 mmol)

and TBSOTf (0.4 mL, 1.74 mmol) at room temperature. After 30 min, additional amounts of 2,6-lutidine (0.2 mL, 1.72 mmol) and TBSOTf (0.4 mL, 1.74 mmol) were added, and stirring was continued for further 20 min. Then the mixture was poured into a separatory funnel where it was partitioned between sat. $NaHCO_3$ and CH_2Cl_2. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (*n*-hexane) to give silyl ether **4** (484 mg, 98%) as a colorless oil. **Silyl ether 4**: colorless oil; $[\alpha]^{22}_D$ +13.1 (*c* 0.95, $CHCl_3$); IR (neat) ν 2957, 2930, 2859, 1464, 1254, 1084, 932, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.84 (ddd, 1H, *J* = 17.4, 10.5, 7.3 Hz), 5.33 (dd, 1H, *J* = 17.4, 1.0 Hz), 5.28 (dd, 1H, *J* = 10.5, 1.0 Hz), 4.55 (t, 1H, *J* = 6.4 Hz), 4.10 (ddd, 1H, *J* = 9.6, 6.9, 2.3 Hz), 4.01 (dd, 1H, *J* = 6.4, 5.5 Hz), 2.00 (m, 1H), 1.79 (m, 1H), 1.60 (m, 1H), 1.42-1.24 (m, 7H), 0.90 (s, 9H), 0.89 (t, 3H, *J* = 6.9), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.5, 118.6, 74.8, 69.4, 62.3, 33.7, 31.7, 28.8, 25.9, 25.77 (overlapped, 2 x C), 25.75, 22.6, 18.1, 14.0, -4.1, -4.9; MS *m/z*: 353 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{17}H_{35}O^{35}Cl_2Si$ $[M+H]^+$ 353.1834, found: 353.1852.



***anti*-3**

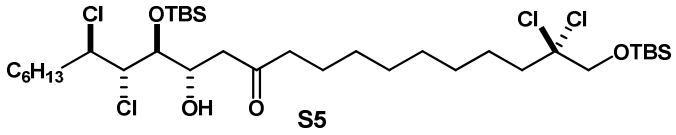


***syn*-3**

(*S*)-5-[(1*S*,2*S*,3*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3-dichlorononyl]-3-[10-(*tert*-butyldimethylsilyl oxy)-9,9-dichlorodecyl]-4,5-dihydroisoxazole (*anti*-3)

(*R*)-5-[(1*S*,2*S*,3*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3-dichlorononyl]-3-[10-(*tert*-butyldimethylsilyl oxy)-9,9-dichlorodecyl]-4,5-dihydroisoxazole (*syn*-3): To a stirred solution of silyl ether **4** (261 mg, 0.739 mmol) in toluene (7.4 mL) were added nitro compound **5** (414 mg, 1.03 mmol), Et_3N (0.31 mL, 2.22 mmol), and phenyl isocyanate (1.0 M in toluene, 75 μL, 0.075 mmol) at room temperature. The mixture was heated at 90 °C. After 1h, an additional amount of phenyl isocyanate (1.0 M in toluene, 75 μL, 0.075 mmol) was added, and the mixture was heated at the same temperature for further 9.7 h. Then, additional amounts of phenyl isocyanate (1.0 M in toluene, 75 μL, 0.075 mmol) were added every 1 h for 14 h* [*The total amount of phenyl isocyanate used for this process was 1.13 mL (1.11 mmol)]. After further 10 h of stirring at the same temperature, phenyl isocyanate (1.0 M in toluene, 75 μL, 0.075 mmol) were again added every 1 h for an additional 14 h. After further 10.5 h of stirring, the mixture was heated for an additional 7.5 h during which time phenyl isocyanate (1.0 M in toluene, 75 μL, 0.075 mmol) was repeatedly added seven times (1 h interval). The mixture was then quenched with MeOH and filtered through a Celite pad. The filtrate was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (toluene/*n*-hexane 2:1) to give a less

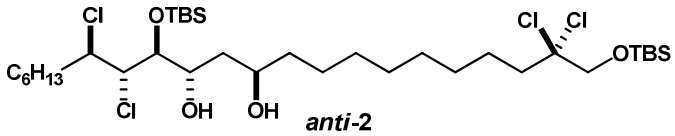
polar *syn*-isoxazoline **3** (41 mg, 7%) as a pale yellow oil and a more polar *anti*-isoxazoline **3** (298 mg, 53%) as a pale yellow oil. ***Anti*-isoxazoline 3**: pale yellow oil; $[\alpha]^{21}_{D}$ +29.0 (*c* 1.09, $CHCl_3$); IR (neat) ν 2953, 2930, 2857, 1464, 1256, 1121, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.81 (dt, 1H, *J* = 9.6, 3.7 Hz), 4.47 (t, 1H, *J* = 4.1 Hz), 4.23 (ddd, 1H, *J* = 9.6, 7.8, 2.3 Hz), 3.95 (dd, 1H, *J* = 7.8, 4.1 Hz), 3.91 (s, 2H), 3.08 (dd, 1H, *J* = 17.4, 9.6 Hz), 2.83 (dd, 1H, *J* = 17.4, 10.5 Hz), 2.36-2.28 (m, 2H), 2.19-2.13 (m, 2H), 2.02 (m, 1H), 1.76 (m, 1H), 1.67-1.51 (m, 3H), 1.44-1.22 (m, 17H), 0.94-0.85 (m, 21H), 0.13 (s, 3H), 0.104 (s, 6H), 0.095 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.3, 93.4, 80.4, 72.1, 71.9, 68.4, 62.0, 43.4, 37.9, 34.2, 31.6, 29.2 , 29.1, 29.0, 28.8, 27.7, 26.3, 25.8 (overlapped, 3 x C), 25.7 (overlapped, 3 x C), 25.6, 24.7, 22.5, 18.2, 18.1, 14.0, -4.3, -4.9, -5.4 (overlapped, 2 x C); ^{13}C NMR (100 MHz, CD_3OD) δ: 161.7, 94.5, 81.8, 73.3, 73.1, 69.4, 63.3, 44.7, 38.6, 35.5, 32.8, 30.3 , 30.22, 30.16, 30.1, 29.9, 28.4, 27.3, 26.7, 26.4 (overlapped, 3 x C), 26.2 (overlapped, 3 x C), 25.9, 23.6, 19.2, 19.1, 14.4, -3.9, -4.6, -5.2 (overlapped, 2 x C); MS *m/z*: 734 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{68}O_3N^{35}Cl_4Si_2$ $[M+H]^+$ 734.3492, found: 734.3486. ***Syn*-isoxazoline 3**: pale yellow oil; $[\alpha]^{22}_{D}$ -29.4 (*c* 0.68, $CHCl_3$); IR (neat) ν 2953, 2928, 2857, 1464, 1256, 1121, 837, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.76 (ddd, 1H, *J* = 10.5, 9.6, 7.3 Hz), 4.28 (ddd, 1H, *J* = 9.6, 7.3, 2.3 Hz), 4.16 (dd, 1H, *J* = 7.3, 3.2 Hz), 4.08 (dd, 1H, *J* = 7.3, 3.2 Hz), 3.92 (s, 2H), 2.97 (dd, 1H, *J* = 16.9, 10.5 Hz), 2.78 (dd, 1H, *J* = 16.9, 9.6 Hz), 2.40-2.25 (m, 2H), 2.20-2.14 (m, 2H), 2.08 (m, 1H), 1.78 (m, 1H), 1.64-1.51 (m, 3H), 1.44-1.23 (m, 17H), 0.92 (s, 9H), 0.91 (s, 9H), 0. 89 (t, 3H, *J* = 6.9 Hz), 0.19 (s, 3H), 0.13 (s, 3H), 0.11(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.8, 93.5, 81.7, 76.8, 72.1, 67.1, 61.3, 43.4, 39.3, 34.8, 31.6, 29.21 , 29.18, 29.10, 29.0, 28.7, 27.7, 26.2, 26.0 (overlapped, 3 x C), 25.7 (overlapped, 3 x C), 25.6, 24.7, 22.6, 18.4, 18.3, 14.0, -4.3, -4.7, -5.4 (overlapped, 2 x C); MS *m/z*: 734 $[M+H]^+$, 155 (100%); HRMS (FAB) calcd for $C_{34}H_{68}O_3N^{35}Cl_4Si_2$ $[M+H]^+$ 734.3492, found: 734.3495.



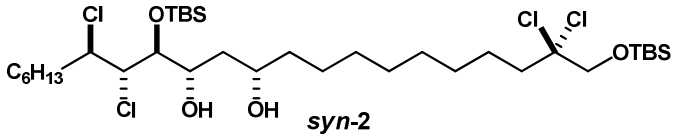
S5

(5*S*,6*S*)-17,17-Dichloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-6-hydroxy-2,2,3,3,20,20,21,21-octamethyl-4, 19-dioxa-3,20-disiladocosan-8-one (S5): To a solution of *anti*-isoxazoline **3** (281 mg, 0.38 mmol) in MeCN (19 mL) at room temperature were added H_2O (1.2 mL) and $Mo(CO)_6$ (121 mg, 0.46 mmol). The mixture was stirred at 90 ^oC for 1.5 h, and silica gel 60N (spherical, neutral) was added to the mixture. After 5 min, the mixture was filtered through a Celite pad, and the filtrate was concentrated. The residue was purified by flash silica gel column chromatography (Et_2O/*n*-hexane 1:20) to give aldol **S5** (228 mg, 81%) as a colorless oil. **Aldol S5**: colorless oil; $[\alpha]^{21}_{D}$ -7.4 (*c* 0.89, $CHCl_3$); IR (neat) ν 3522, 2928, 2857, 1732, 1713, 1464, 1260, 1117, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.51 (ddd, 1H, *J* = 9.2, 7.3, 2.3 Hz), 4.40 (ddd, 1H, *J* = 11.9, 6.0, 3.2 Hz), 4.21 (dd, 1H, *J* = 6.0, 4.6

Hz), 4.05 (dd, 1H, *J* = 7.3, 4.6 Hz), 3.92 (s, 2H), 3.32 (d, 1H, *J* = 3.7 Hz), 2.79 (dd, 1H, *J* = 17.9, 2.3 Hz), 2.58 (dd, 1H, *J* = 17.9, 9.2 Hz), 2.48-2.39 (m, 2H), 2.20-2.13 (m, 2H), 2.01 (m, 1H), 1.75 (m, 1H), 1.69-1.50 (m, 3H), 1.44-1.20 (m, 17H), 0.96-0.84 (m, 21H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 212.6, 93.5, 74.6, 72.1, 68.8, 68.6, 62.7, 44.3, 43.7, 43.5, 34.2, 31.6, 29.19, 29.17, 29.06, 29.0, 28.8, 25.9 (overlapped, 3 x C), 25.7 (overlapped, 3 x C), 25.6, 24.7, 23.6, 22.5, 18.3, 18.1, 14.0, -4.1, -4.6, -5.4 (overlapped, 2 x C); MS *m/z*: 739 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{69}O_4{}^{35}Cl_3{}^{37}ClSi_2$ $[M+H]^+$ 739.3459, found: 739.3476.



***anti*-2**

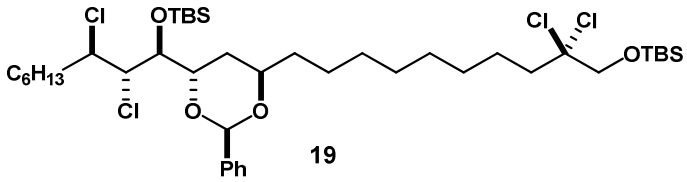


***syn*-2**

(5*S*,6*S*,8*R*)-17,17-Dichloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocosane-6,8-diol (*anti*-2)

(5*S*,6*S*,8*S*)-17,17-Dichloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocosane-6,8-diol (*syn*-2): To a stirred suspension of $Me_4NHB(OAc)_3$ (695 mg, 2.64 mmol) in CH_3CN (1.5 mL) was added AcOH (1.5 mL) at room temperature, and the mixture was stirred for 40 min. To this mixture was added a solution of aldol **S5** (202 mg, 0.273 mmol) in $MeCN/CH_2Cl_2$ (2 mL; 3:1 v/v). After 1h, 0.5 M aqueous solution of sodium potassium tartrate (10 mL) was added, and stirring was continued for further 5 min. The mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (Et_2O/*n*-hexane 1:20) to give a less polar *syn*-diol **2** (24.3 mg, 12 %) as a pale yellow oil and a more polar *anti*-diol **2** (145 mg, 72 %) as a pale yellow oil. ***Anti*-diol 2**: pale yellow oil; $[\alpha]^{21}{}_D$ +6.5 (*c* 0.84, $CHCl_3$); IR (neat) ν 3383, 2928, 2857, 1464, 1256, 1119, 837, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.57 (ddd, 1H, *J* = 9.6, 6.4, 2.3 Hz), 4.23 (ddd, 1H, *J* = 8.5, 5.0, 2.7 Hz), 4.18-4.12 (m, 2H), 3.98 (m, 1H), 3.92 (s, 2H), 2.32 (brs, 1H), 2.23-2.12 (m, 2H), 2.03 (m, 1H), 1.83-1.49 (m, 8H), 1.44-1.20 (m, 17H), 0.91 (s, 18H), 0.88 (t, 3H, *J* = 6.9 Hz), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 93.5, 75.7, 72.1, 70.2, 69.8, 68.7, 63.1, 43.5, 37.4, 37.2, 34.1, 31.6, 29.5, 29.4, 29.3, 29.0, 28.9, 25.9 (overlapped, 3 x C), 25.8, 25.7 (overlapped, 3 x C), 24.7, 22.5, 18.2, 18.1, 14.0, -4.1, -4.5, -5.4 (overlapped, 2 x C); ^{13}C NMR (125 MHz, CD_3OD) δ: 94.5, 78.7, 73.2, 70.3, 70.0, 69.0, 64.0, 44.8, 40.4, 39.1, 35.0, 32.9, 30.7, 30.5, 30.4, 30.1, 30.0, 27.1, 26.7, 26.6 (overlapped, 3 x C), 26.2 (overlapped, 3 x C), 25.9, 23.6, 19.2, 19.1, 14.4, -3.5, -4.2, -5.2 (overlapped, 2 x C); MS *m/z*: 763 $[M+Na]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{70}O_4{}^{35}Cl_3{}^{37}ClSi_2Na$ $[M+Na]^+$ 763.3435, found: 763.3463. ***Syn*-diol 2**: pale yellow oil; $[\alpha]^{22}{}_D$ +9.9

(*c* 0.79, $CHCl_3$); IR (neat) ν 3391, 2928, 2857, 1464, 1256, 1119, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.57 (ddd, 1H, *J* = 10.1, 6.4, 2.3 Hz), 4.17 (ddd, 1H, *J* = 10.1, 5.5, 1.4 Hz) 4.13 (dd, 1H, *J* = 6.4, 4.6 Hz), 4.04 (dd, 1H, *J* = 5.5, 4.6 Hz), 3.92 (s, 2H), 3.90 (m, 1H), 2.59 (brs, 1H), 2.21-2.13 (m, 2H), 2.02 (m, 1H), 1.85-1.71 (m, 2H), 1.66-1.15 (m, 23H), 0.91 (s, 18H), 0.88 (t, 3H, *J* = 6.9 Hz), 0.144 (s, 3H), 0.136 (s, 3H), 0.11(s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 93.5, 76.2, 74.1, 73.5, 72.1, 68.6, 62.9, 43.5, 38.6, 38.2, 34.1, 31.7, 29.7, 29.5, 29.4, 29.3, 29.0, 28.9, 25.9 (overlapped, 2 x C), 25.8, 25.7 (overlapped, 3 x C), 25.3, 24.8, 22.6, 18.3, 18.2, 14.0, -4.1, -4.5, -5.4 (overlapped, 2 x C); MS *m/z*: 763 $[M+Na]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{70}O_4{}^{35}Cl_3{}^{37}ClSi_2Na$ $[M+Na]^+$ 763.3435, found: 763.3433.

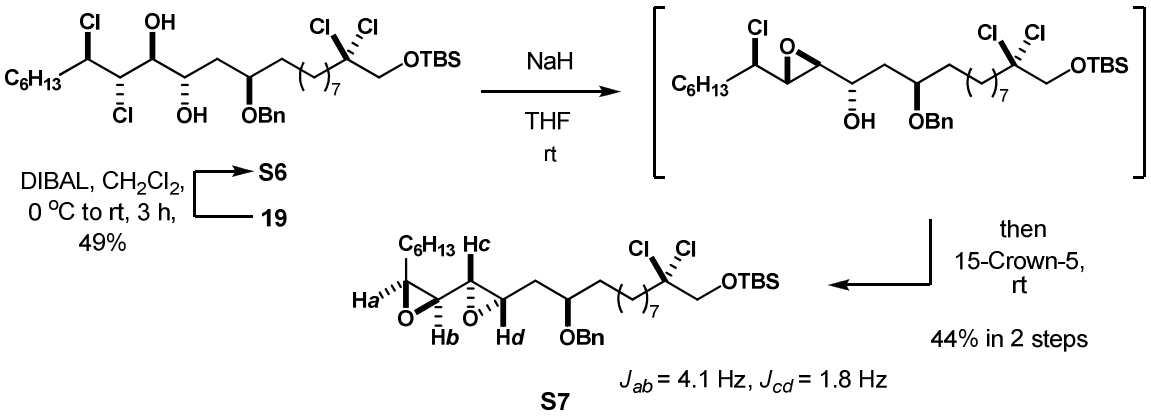


19

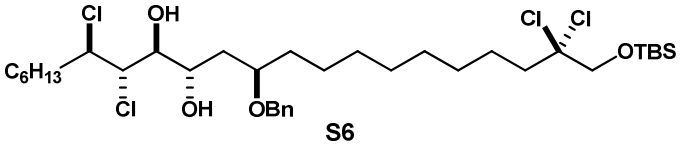
***tert*-Butyl(10-{(2*R*,4*R*,6*S*)-6-[(1*S*,2*S*,3*R*)-1-(*tert*-butyldimethylsilyloxy)-2,3-dichlorononyl]-2-phenyl-1,3-dioxan-4-yl}-2,2-dichlorodecyloxy)dimethylsilane (19)**: To a stirred solution of *anti*-diol **2** (21 mg, 0.0283 mmol) in CH_2Cl_2 (1.0 mL) at room temperature were added benzaldehyde dimethylacetal (0.43 mL, 0.0425 mmol) and PPTS (7 mg, 0.0283 mmol). After 70 min, an additional amount of benzaldehyde dimethylacetal (0.43 mL, 0.0425 mmol) was added. The mixture was stirred at the same temperature for 100 min, during which time further amount of benzaldehyde dimethylacetal (0.43 mL, 0.0425 mmol) was added twice. The mixture was poured into a separatory funnel where it was partitioned between sat. $NaHCO_3$ and CH_2Cl_2. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (Et_2O/*n*-hexane 1:20) to give acetal **19** (23 mg, 97%) as a colorless oil. **Acetal 19**: colorless oil; $[\alpha]^{21}{}_D$ +15.4 (*c* 0.66, $CHCl_3$); IR (neat) ν 2953, 2928, 2857, 1734, 1462, 1362, 1256, 1117, 839, 777, 696 cm^{-1};^1H NMR (500 MHz, $CDCl_3$) δ: 7.53-7.45 (m, 2H), 7.39-7.30 (m, 3H), 5.89 (s, 1H), 4.98 (dd, 1H, *J* = 9.2, 1.2 Hz), 4.54 (ddd, 1H, *J* = 9.2, 6.1, 1.8 Hz), 4.42 (dt, 1H, *J* = 9.8, 2.4 Hz), 4.18 (dd, 1H, *J* = 9.8, 1.2 Hz), 3.92 (s, 2H), 3.90 (m, 1H), 2.21-2.10 (m, 3H), 1.97 (brd, 1H, *J* = 14.0 Hz), 1.83 (ddd, 1H, *J* = 13.4, 11.6, 6.7 Hz), 1.77-1.63 (m, 2H), 1.63-1.43 (m, 4H), 1.42-1.17 (m, 17H), 0.94 (s, 9H), 0.91 (s, 9H), 0.86 (t, 3H, *J* = 6.7 Hz), 0.21 (s, 3H), 0.15 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.8, 128.8, 128.3 (overlapped, 2 x C), 126.1 (overlapped, 2 x C), 96.7, 93.5, 73.2, 72.4, 72.1, 70.2, 67.9, 62.7, 43.5, 36.2, 35.4, 31.6, 29.8, 29.6, 29.4, 29.3, 29.0, 28.5, 25.73 (overlapped, 3 x C), 25.71 (overlapped, 3 x C), 25.0, 24.80, 24.75, 22.5, 18.3, 18.0, 14.1, -4.0, -4.4, -5.4 (overlapped, 2 x C); MS *m/z*: 849 $[M+Na]^+$, 73 (100%); HRMS (FAB) calcd for $C_{41}H_{74}O_4{}^{35}Cl_4Si_2Na$ $[M+Na]^+$ 849.3778, found: 849.3769.

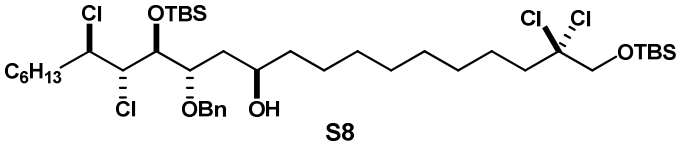
Determination of the stereochemistry of the C13~C16 centers of compound 19 via sequential Payne rearrangement.

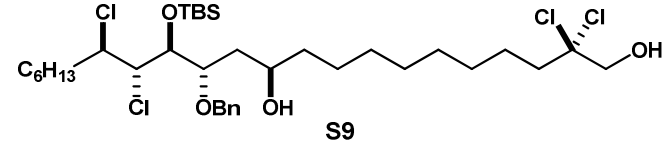
SI Scheme 1. Determination of stereochemistry of the C13~C16 centers via sequential Payne rearrangement.

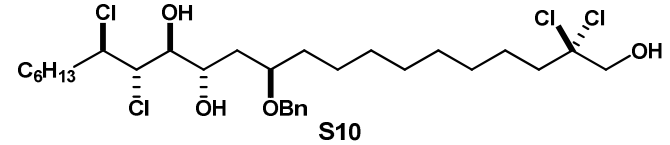


The transformation of benzylidene acetal **19** into bisepoxide **S7** allowed us to establish all the relative stereochemistry at the C11~C13 positions. Reductive opening of the acetal moiety of compound **19** with DIBAL in CH_2Cl_2 at 0 °C to room temperature delivered diol **S6**, which was unexpectedly produced by concomitant removal of the secondary TBS group during the reaction. Diol **S6** was then subjected to sequential Payne rearrangement by treatment with NaH in THF at room temperature to afford an epoxy alcohol which, upon further stirring in the presence of 15-crown-5, gave bisepoxide **S7** in 44% overall yield from **S6**. The analysis of the coupling constants of bisepoxide **S7** showed *cis* relationship (J_{ab} = 4.1 Hz) between the C15 and C16 protons and *trans* relationship (J_{cd} = 1.8 Hz) between C13 and C14 protons, respectively, indicating that *anti*-diol **2** possessed the configuration suitable for accessing natural danicalipin A (**1**).


S6


S8


S9


S10

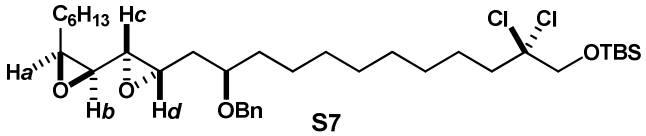
(7*R*,8*S*,9*S*,10*S*,12*R*)-12-(Benzyloxy)-22-(*tert*-butyldimethylsilyloxy)-7,8,21,21-tetrachlorodocosane-9,10-diol (S6)

(5*S*,6*S*,8*R*)-6-(Benzyloxy)-17,17-dichloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocosan-8-ol (S8)

(11*R*,13*S*,14*S*,15*S*,16*R*)-13-(Benzyloxy)-14-(*tert*-butyldimethylsilyloxy)-2,2,15,16-tetrachlorodocosane-1,11-diol (S9)

(11*R*,13*S*,14*S*,15*S*,16*R*)-11-(Benzyloxy)-2,2,15,16-tetrachlorodocosane-1,13,14-triol (S10): To a solution of benzylidene acetal **19** (14.5 mg, 0.0175 mmol) in CH_2Cl_2 (1.0 mL) at 0 ^oC was added DIBAL (1.03 M in *n*-hexane, 0.17 mL, 0.175 mmol). After 3 h, 28% NH_4OH was added, and the mixture was allowed to warm to room temperature. After 15 min, Celite was added and the whole mixture was stirred for an additional 2 h. After filtration of the mixture through a Celite pad followed by concentration of the filtrate under reduced pressure, the residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:15) to give alcohol **S8** (2.2 mg, 15%) as a colorless oil. Further elution with EtOAc/*n*-hexane (1:10 to 1:4) gave a less polar diol **S6** (6.2 mg, 49%) as a colorless oil, a more polar diol **S9** (0.9 mg, 7%) as a colorless oil, and most polar triol **S10** (2.5 mg, 24%) as a colorless oil. **Diol S6**: colorless oil; $[\alpha]^{19}_D$ +12.4 (*c* 0.10, $CHCl_3$); IR (neat) ν 3412, 2926, 2855, 1730, 1464, 1258, 1119, 1067, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.40-7.28 (m, 5H), 4.60 (d, 1H, *J* = 11.4 Hz), 4.55 (m, 1H), 4.52 (d, 1H, *J* = 11.4 Hz), 4.27 (m, 1H), 4.12 (dd, 1H, *J* = 8.2, 3.7 Hz), 3.92 (s, 2H), 3.91 (m, 1H), 3.79 (m, 1H), 2.69 (d, 1H, *J* = 3.2 Hz) 2.21-2.14 (m, 2H), 2.03-1.74 (m, 4H), 1.69-1.53 (m, 5H), 1.46-1.20 (m, 17H), 0.91 (s, 9H), 0.89 (t, 3H, *J* = 6.9 Hz), 0.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.8, 128.6 (overlapped, 2 x C), 128.0, 127.9 (overlapped, 2 x C), 93.5, 77.8, 73.8, 72.1, 71.2, 69.0, 66.8, 62.8, 43.5, 32.6, 32.3, 31.6, 29.7, 29.6, 29.35, 29.30, 29.0, 28.7, 26.3, 25.7 (overlapped, 3 x C), 25.6, 24.8, 22.6, 18.3, 14.0, -5.3 (overlapped, 2 x C); MS *m/z*: 715 $[M+H]^+$, 91 (100%); HRMS (FAB) calcd for $C_{35}H_{63}O_4{}^{35}Cl_4Si$ $[M+H]^+$ 715.3250, found: 715.3256. **Diol S8**: colorless oil; $[\alpha]^{23}_D$ -2.1 (*c* 0.14, $CHCl_3$); IR (neat) ν 3509, 2955, 2928, 2857, 1732, 1464, 1257, 1119, 1074, 837, 777 cm^{-1};^1H NMR (500 MHz, $CDCl_3$) δ: 7.37-7.28 (m, 5H), 4.65 (d, 1H, *J* = 11.6 Hz), 4.57 (d, 1H, *J* = 11.6 Hz), 4.44 (ddd, 1H, *J* = 9.8, 5.5, 2.4 Hz), 4.27 (dd, 1H, *J* = 6.7, 3.7 Hz), 4.12 (m, 1H), 4.07 (t, 1H, *J* = 5.5 Hz), 3.92 (s, 2H), 3.79 (m, 1H), 2.20-2.14 (m, 2H), 1.95-1.72 (m, 4H), 1.66-1.19 (m, 22H), 0.94-0.82 (m, 21H), 0.12 (s, 3H), 0.11 (s, 6H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.5, 128.2 (overlapped, 2 x C), 127.9 (overlapped, 2 x C), 127.7, 93.3, 77.7, 73.5, 72.0, 71.9, 68.3, 68.1, 62.6, 43.3, 37.7, 35.5, 32.8, 31.4, 29.3, 29.2, 29.1, 28.8, 28.7, 25.9, 25.8, 25.7 (overlapped, 3 x C), 25.5 (overlapped, 3 x C), 25.4, 24.5, 22.3, 18.0, 13.8, -3.9, -5.3, -5.6 (overlapped, 2 x C); MS *m/z*: 831 $[M+H]^+$, 91 (100%); HRMS (FAB) calcd for $C_{41}H_{77}O_4{}^{35}Cl_3{}^{37}ClSi_2$ $[M+H]^+$ 831.4085, found: 831.4080. **Diol S9**: colorless oil; $[\alpha]^{23}_D$ +3.7 (*c* 0.04, $CHCl_3$); IR (neat) ν 3420, 2928, 2855, 1722, 1464, 1256, 1117, 1066, 835, 777 cm^{-1};^1H NMR (500 MHz, $CDCl_3$) δ: 7.37-7.29 (m, 5H), 4.65 (d, 1H, *J* = 11.0 Hz), 4.56 (d, 1H, *J* = 11.0 Hz), 4.44 (ddd, 1H, *J* = 10.3, 5.5, 2.4 Hz), 4.26 (dd, 1H, *J* = 6.7, 3.7 Hz), 4.12 (dt, 1H, *J* = 8.6, 3.7 Hz), 4.06 (dd, 1H, *J* = 6.7, 5.5 Hz), 3.90 (d, 2H, *J* = 7.3 Hz), 3.79 (m, 1H), 2.34 (t, 1H, *J* = 7.3 Hz), 2.23-2.18 (m, 2H), 1.94 (brs, 1H), 1.82 (m, 1H), 1.78 (ddd, 2H, *J* = 14.6, 8.5, 1.8 Hz), 1.69-1.20 (m, 23H), 0.90 (s, 9H), 0.89 (t, 3H, *J* = 6.7 Hz), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.7, 128.5 (overlapped, 2 x C), 128.2 (overlapped, 2 x C), 127.9, 94.7, 77.9, 73.7, 72.2, 72.1, 68.5, 68.3, 62.9, 43.5, 37.9, 35.7, 33.0, 31.7, 29.5, 29.4, 29.3, 29.0

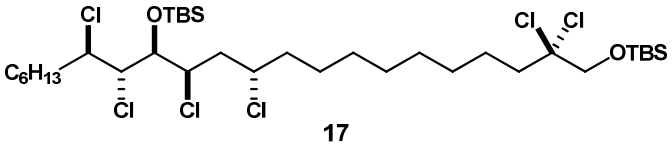
(overlapped, 2 x C), 26.2, 26.0 (overlapped, 3 x C), 25.6, 24.8, 22.5, 18.3, 14.0, -3.6, -5.1; MS *m/z*: 717 $[M+H]^+$, 91 (100%); HRMS (FAB) calcd for $C_{35}H_{63}O_4{}^{35}Cl_3{}^{37}ClS_i$ $[M+H]^+$ 717.3220, found: 717.3248. **Triol S10**: colorless oil; $[\alpha]^{23}_D$ +7.7 (*c* 0.15, $CHCl_3$); IR (neat) ν 3404, 2928, 2855, 1715, 1454, 1065, 746, 698 cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.28 (m, 5H), 4.59 (d, 1H, *J* = 11.6 Hz), 4.55 (m, 1H), 4.53 (d, 1H, *J* = 11.6 Hz), 4.27 (ddd, 1H, *J* = 9.8, 4.3, 2.4 Hz), 4.12 (dd, 1H, *J* = 8.5, 3.7 Hz), 3.91 (m, 1H), 3.90 (s, 2H), 3.78 (m, 1H), 2.69 (brs, 1H), 2.35 (m, 1H), 2.24-2.16 (m, 2H), 1.99-1.74 (m, 4H), 1.69-1.19 (m, 23H), 0.92-0.83 (m, 3H) ; ^{13}C NMR (125 MHz, CD_3OD) δ: 140.2, 129.3 (overlapped, 2 x C), 129.1 (overlapped, 2 x C), 128.6, 95.7, 77.7, 77.0, 72.6, 72.4, 70.2, 68.9, 64.1, 44.6, 37.3, 35.5, 34.0, 32.9, 30.8, 30.5, 30.4, 30.2, 29.8, 27.5, 26.3, 25.9, 23.6, 14.4; MS *m/z*: 625 $[M+Na]^+$, 57 (100%); HRMS (FAB) calcd for $C_{29}H_{48}O_4{}^{35}Cl_3{}^{37}ClNa$ $[M+Na]^+$ 625.2175, found: 625.2180.



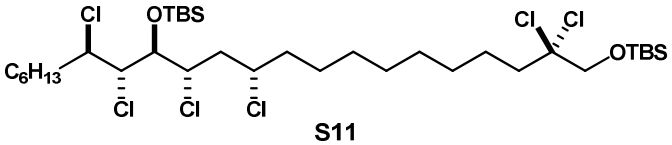
S7

J_{ab} = 4.1 Hz J_{cd} = 1.8 Hz

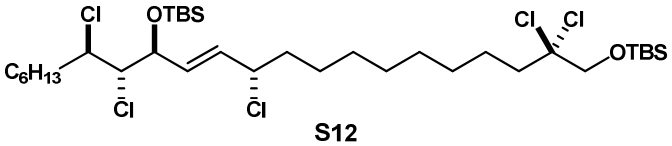
{(*R*)-11-(Benzyloxy)-2,2-dichloro-12-[(2*R*,2'*S*,3*S*,3'*S*)-3'-hexyl-2,2'-bioxiran-3-yl]dodecyloxy}(*tert*-butyl)dimethylsilane (S7): To a stirred solution of diol **S6** (8.3 mg, 0.012 mmol) in THF (1.0 mL) at 0 ^{o}C was added NaH (60% in oil, 1.4 mg, 0.036 mmol). After 75 min, 15-crown-5 (7.1 μL, 0.036 mmol) was added, and the mixture was stirred at room temperature for 6.3 h. The mixture was poured into a separatory funnel where it was partitioned between Et_2O and sat. NH_4Cl. The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:15) to give epoxide **S7** (3.4 mg, 44%) as a pale yellow oil. **Epoxide S7**: pale yellow oil; $[\alpha]^{26}_D$ -5.5 (*c* 0.13, $CHCl_3$); IR (neat) ν 2928, 2857, 1738, 1464, 1258, 1153, 1117, 1071, 839, 779 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39-7.24 (m, 5H), 4.60 (s, 2H), 3.92 (s, 2H), 3.63 (m, 1H), 3.15 (ddd, 1H, *J* = 7.3, 4.1, 1.8 Hz), 3.01 (dt, 1H, *J* = 6.4, 4.1 Hz), 2.73 (dd, 1H, *J* = 6.9, 4.1 Hz), 2.68 (dd, 1H, *J* = 6.9, 1.8 Hz), 2.20-2.14 (m, 2H), 1.90 (ddd, 1H, *J* = 14.7, 8.2, 4.1 Hz), 1.67-1.45 (m, 8H), 1.43-1.17 (m, 17H), 0.91 (s, 9H), 0.89 (t, 3H, *J* = 6.9 Hz), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.6, 128.4 (overlapped, 2 x C), 127.8 (overlapped, 2 x C), 127.6, 93.5, 76.7, 72.1, 71.4, 57.0, 55.4, 55.3, 55.1, 43.5, 36.8, 34.3, 31.7, 29.7 , 29.4, 29.3, 29.1, 29.0, 28.1, 26.5, 25.7 (overlapped, 3 x C), 25.1, 24.8, 22.5, 18.3, 14.1, -5.4 (overlapped, 2 x C); MS *m/z*: 665 $[M+Na]^+$, 91 (100%); HRMS (FAB) calcd for $C_{35}H_{60}O_4{}^{35}Cl_2SiNa$ $[M+Na]^+$ 665.3536, found: 665.3533.



17



S11



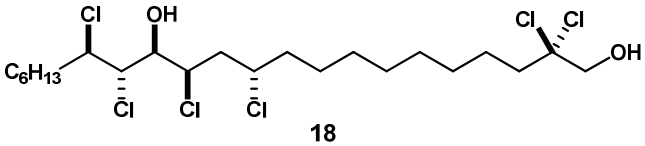
S12

(5*S*,6*R*,8*S*)-6,8,17,17-Tetrachloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocosane (17)

(5*S*,6*S*,8*S*)-6,8,17,17-Tetrachloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocosane (S11)

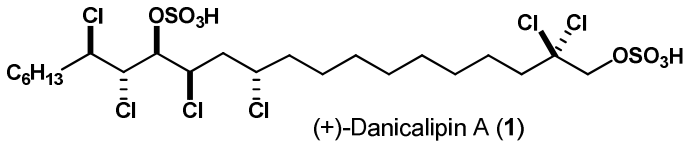
(5*S*,8*S*,*E*)-8,17,17-Trichloro-5-[(1*S*,2*R*)-1,2-dichlorooctyl]-2,2,3,3,20,20,21,21-octamethyl-4,19-dioxa-3,20-disiladocos-6-ene (S12): To a stirred solution of *anti*-diol **2** (132 mg, 0.178 mmol) in 1,2-dichloroethane (1.8 mL) at room temperature were added Ph_3P (140 mg, 0.534 mmol) and NCS (71.4 mg, 0.534 mmol). After being heated at 90 ^oC for 50 min, the mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (*n*-hexane) to give a less polar hexachloride **S11** (7.3 mg, 5%) as a colorless oil, a more polar hexachloride **17** (52.7 mg, 38%) as a colorless oil, and most polar olefin **S12** (52.7 mg, 40%) as a colorless oil. **Hexachloride 17**: colorless oil; $[\alpha]^{21}_D$ +21.0 (*c* 1.35, $CHCl_3$); IR (neat) ν 2953, 2930, 2857, 1464, 1258, 1121, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.69 (d, 1H, *J* =11.4 Hz), 4.39-4.33 (m, 2H), 4.20 (m, 1H), 4.01 (dd, 1H, *J* = 6.9, 1.4 Hz), 3.92 (s, 2H), 2.22-2.13 (m, 3H), 1.96-1.21 (m, 25H), 0.94 (s, 9H), 0.91 (s, 9H), 0.88 (t, 3H, *J* = 6.4 Hz), 0.16 (s, 3H), 0.14 (s, 3H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 93.5, 76.6, 72.1, 67.7, 62.0, 61.4, 60.5, 43.9, 43.5, 38.9, 32.8, 31.6, 29.7, 29.3, 29.2, 29.01, 28.97, 26.5, 26.4, 26.0 (overlapped, 3 x C), 25. 7 (overlapped, 3 x C), 24.7, 22.5, 18.5, 18.2, 14.0, -3.6, -3.8, -5.4 (overlapped, 2 x C); MS *m/z*: 775 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{69}O_2{}^{35}Cl_6Si_2$ $[M+H]^+$ 775.2967, found: 775.2972. **Hexachloride S11**: colorless oil; $[\alpha]^{21}_D$ +20.4 (*c* 0.06, $CHCl_3$); IR (neat) ν 2953, 2928, 2857, 1464, 1258, 1119, 839, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.45-4.35 (m, 2H), 4.28 (dd, 1H, *J* = 6.0, 4.1 Hz), 4.22-4.15 (m, 2H), 3.92 (s, 2H), 2.38 (ddd, 1H, *J* = 14.7, 8.2, 4.1 Hz), 2.28-2.14 (m, 3H), 1.93-1.74 (m, 3H), 1.70-1.21 (m, 21H), 0.97-0.83 (m, 21H), 0.21 (s, 3H), 0.15 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 93.5, 77.1, 72.1, 67.7, 62.2, 60.05, 60.02, 43.5, 41.9, 36.3, 33.4, 31.6, 29.7, 29.29, 29.27, 29.01, 28.98, 28.90, 25.9 (overlapped, 3 x C), 25.8, 25.7 (overlapped, 3 x C), 24.8, 22.5, 18.31, 18.27, 14.0, -3.7, -4.5, -5.3 (overlapped, 2 x C); MS *m/z*: 775 $[M+H]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{69}O_2{}^{35}Cl_6Si_2$ $[M+H]^+$ 775.2967, found: 775.2963. This compound was tentatively assigned as (11*S*, 13*S*)-*syn*-isomer (danicalipin numbering) that was likely to be produced through the anchimeric

assistance of the neighboring chlorine atom. **Olefin S12**: colorless oil; $[\alpha]^{22}_{D}$ +10.5 (*c* 0.25, $CHCl_3$); IR (neat) ν 2953, 2928, 2857, 1464, 1258, 1119, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 5.84 (dd, 1H, *J* =15.6, 7.8 Hz), 5.74 (dd, 1H, *J* =15.6, 6.4 Hz), 4.63 (dd, 1H, *J* = 6.4, 4.1 Hz), 4.38 (dt, 1H, *J* = 7.3, 7.3 Hz), 4.05-3.97 (m, 2H), 3.92 (s, 2H), 2.21-2.13 (m, 2H), 2.02 (m, 1H), 1.89-1.72 (m, 3H), 1.70-1.25 (m, 20H), 0.913 (s, 9H), 0.906 (s, 9H), 0.89 (t, 3H, *J* = 6.9 Hz), 0.11 (s, 6H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.7, 130.1, 93.4, 73.0, 72.1, 69.6, 62.2, 61.8, 43.5, 38.3, 33.8, 31.6, 29.7, 29.29, 29.25, 29.0, 28.9, 28.7, 26.4, 25.74 (overlapped, 3 x C), 25.71 (overlapped, 3 x C), 24.7, 22.5, 18.2, 18.1, 14.0, -4.1, -4.9, -5.4 (overlapped, 2 x C); MS *m/z*: 761 $[M+Na]^+$, 73 (100%); HRMS (FAB) calcd for $C_{34}H_{67}O_2{}^{35}Cl_5Si_2Na$ $[M+Na]^+$ 761.3020, found: 761.3007.



18

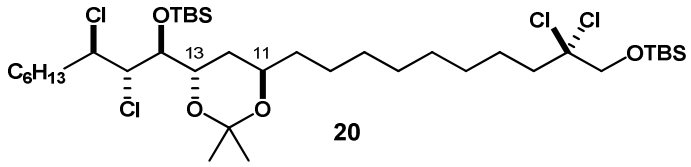
(11*S*,13*R*,14*S*,15*S*,16*R*)-2,2,11,13,15,16-Hexachlorodocosane-1,14-diol (18): To a stirred solution of hexachloride **17** (7.0 mg, 0.009 mmol) in MeOH (1.0 mL) at room temperature was added AcCl (30 μl, 0.42 mmol), and the mixture was heated at 80 °C. After 2 h, an additional AcCl (30 μl, 0.42 mmol) was added. Then the mixture was stirred for further 18 h during which time additional amount of AcCl (30 μl, 0.42 mmol) was added twice. The mixture was concentrated under reduced pressure, diluted with CH_2Cl_2, and poured into a separatory funnel where it was partitioned between CH_2Cl_2 and water. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (EtOAc/*n*-hexane 1:10) to give diol **18** (4.8 mg, 97%) as a pale yellow oil. The spectroscopic and analytical data of this material were in good agreement with those recorded in the literature.[2a,b] **Diol 18**: pale yellow oil; $[\alpha]^{25}_{D}$ +33.1 (*c* 0.71, MeOH) [lit.[2a] $[\alpha]^{22}_{D}$ +35.9 (*c* 0.005, MeOH)] IR (neat) ν 3412, 2930, 2857, 1464, 1379, 1244, 1067, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.96 (d, 1H, *J* = 10.1 Hz), 4.51 (dt, 1H, *J* = 10.5, 2.7 Hz), 4.30 (dd, 1H, *J* = 9.6, 2.7 Hz), 4.15 (m, 1H), 3.91 (d, 2H, *J* = 6.4 Hz), 3.77 (brt, 1H, *J* = 10.5 Hz), 2.37-2.27 (m, 2H), 2.24-2.18 (m, 2H), 2.19 (d, 1H, *J* = 11.5 Hz), 1.98 (ddd, 1H, *J* = 15.1, 11.0, 2.3 Hz), 1.89 (m, 1H), 1.83-1.72 (m, 3H), 1.70-1.20 (m, 20H), 0.89 (t, 3H, *J* = 6.9 Hz); ^1H NMR (400 MHz, CD_3OD) δ: 4.77 (dt, 1H, *J* = 11.0, 1.8 Hz), 4.56 (ddd, 1H, *J* = 8.2, 4.1, 2.3 Hz), 4.37 (dd, 1H, *J* = 10.1, 2.3 Hz), 4.20 (m, 1H), 3.84 (s, 2H), 3.75 (dd, 1H, *J* = 9.6, 1.4 Hz), 2.32 (ddd, 1H, *J* = 15.1, 11.5, 2.3 Hz), 2.21-2.15 (m, 2H), 1.94 (ddd, 1H, *J* = 15.1, 11.0, 2.3 Hz), 1.86-1.74 (m, 4H), 1.69-1.22 (m, 20H), 0.91 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 94.6, 75.1, 72.1, 66.5, 63.0, 62.7, 60.4, 44.3, 43.5, 38.7, 32.5, 31.6, 29.22, 29.16, 28.9 (overlapped, 2 x C), 28.6, 26.6, 26.2, 24.8, 22.5, 14.0; ^{13}C NMR (125 MHz, CD_3OD) 95.6, 75.6, 72.6, 68.5, 63.9, 63.6, 62.1, 45.3, 44.6, 39.9, 33.0, 32.8, 30.37, 30.35, 30.1, 30.0, 29.7, 27.9, 27.4, 25.9, 23.6, 14.3; MS *m/z*: 549 $[M+H]^+$, 154 (100%); HRMS (FAB) calcd for $C_{22}H_{41}O_2{}^{35}Cl_5{}^{37}Cl$ $[M+H]^+$ 549.1208, found: 549.1201.



(+)-Danicalipin A (**1**)

(+)-Danicalipin A (1): To a stirred solution of diol **18** (7.7 mg, 0.014 mmol) in DMF (0.8 mL) at room temperature was added 50% SO_3·Py (22.3 mg, 0.07 mmol). After 1 h, the mixture was directly filtered through a short plug of silica gel (MeOH/CH_2Cl_2 1:10),** and then the filtrate was concentrated under reduced pressure. **This filtration that ensures the removal of the residual reagents prior to the second chromatographic purification was essential for the successful isolation of danicalipin A. The problematic desulfation of danicalipin observed during chromatographic process was almost completely suppressed by this protocol. The residue was purified by flash silica gel column chromatography (MeOH/CH_2Cl_2 1:5) to give (+)-danicalipin A (**1**) (9.3 mg, 94%) as a colorless gum. **(+)-Daniclipin A (1)**: colorless gum; $[\alpha]^{26}_D$ +33.0 (*c* 0.40, MeOH) [lit.[2a] $[\alpha]^{25}_D$ +12.8 (*c* 0.2, MeOH); lit.[2b] $[\alpha]^{24}_D$ +38 (*c* 0.78, solvent not indicated)]; IR (neat) ν 3460, 2924, 2855, 1728, 1454, 1260, 1015, 831 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ: 4.88 (brd, 1H, *J* = 11.6 Hz), 4.75 (brd, 1H, *J* = 11.0 Hz), 4.53 (dd, 1H, *J* = 10.4 Hz), 4.45 (dd, 1H, *J* = 10.4, 1.2 Hz), 4.29 (s, 2H), 4.21 (m, 1H), 2.52 (ddd, 1H, *J* = 15.3, 11.6, 1.8 Hz), 2.28-2.20 (m, 2H), 2.09 (ddd, 1H, *J* = 15.3, 11.1, 1.8 Hz), 1.94 (m, 1H), 1.84-1.22 (m, 23H), 0.90 (t, 3H, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, CD_3OD) δ: 91.4, 80.9, 75.5, 68.5, 63.4, 62.4, 62.3, 45.5, 45.1, 39.9, 33.5, 32.9, 30.48, 30.45, 30.15, 30.11, 30.09, 27.7, 27.5, 25.8, 23.6, 14.4 ; MS *m/z*: 727 $[M+Na-2H]^-$, 153 (100%); HRMS (FAB) calcd for $C_{22}H_{38}O_8{}^{35}Cl_6S_2Na$ $[M+Na-2H]^-$ 727.0037, found: 727.0037. The spectroscopic and analytical data of this material were in good agreement with those reported. [2a,b]

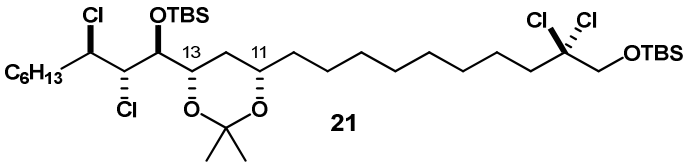
Determination of stereochemistry at the C11 and C13 positions:



20

***tert*-Butyl(10-{(4*R*,6*S*)-6-[(1*S*,2*S*,3*R*)-1-(*tert*-butyldimethylsilyloxy)-2,3-dichlorononyl]-2,2-dimethyl-1,3-dioxan-4-yl}-2,2-dichlorodecyloxy)dimethylsilane (20)**: To a stirred solution of *anti*-diol **2** (11.1 mg, 0.015 mmol) in CH_2Cl_2 (1 mL) at room temperature were added 2,2-dimethoxypropane (9.2 μl, 0.075 mmol) and PPTS (2 mg, 0.088 mmol). After 8.8 h, the mixture was heated at reflux for 110 min. Additional amounts of 2,2-dimethoxypropane (9.2 μl, 0.075 mmol) and PPTS (2 mg, 0.088 mmol) were added, and the mixture was heated at reflux for further 1 h. The mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (Et_2O/*n*-hexane 1:50) to give acetal **20** (9.9 mg, 85%) as a pale yellow oil. **Acetal 20**: pale yellow oil; $[\alpha]^{25}_D$ -1.4 (*c* 0.46, $CHCl_3$); IR (neat) ν 2953,

2930, 2857, 1464, 1379, 1256, 1225, 1119, 837, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.43 (ddd, 1H, *J* = 10.1, 6.0, 2.3 Hz), 4.20 (ddd, 1H, *J* = 9.6, 6.0, 5.0 Hz), 4.13 (dd, 1H, *J* = 5.5, 5.0 Hz), 4.02 (dd, 1H, *J* = 6.0, 5.5 Hz), 3.92 (s, 2H), 3.72 (m, 1H), 2.21-2.13 (m, 2H), 1.99-1.83 (m, 2H), 1.77 (m, 1H), 1.67-1.23 (m, 23H), 1.34 (s, 3H), 1.32 (s, 3H), 0.93-0.87 (m, 21H), 0.13 (s, 3H), 0.113 (s, 3H), 0.108 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 100.6, 93.5, 75.2, 72.1, 68.0, 67.3, 66.9, 62.6, 43.5, 35.9, 33.5, 33.3, 31.6, 29.5, 29.4, 29.3, 29.0, 28.8, 25.93 (overlapped, 3 x C), 25.91, 25.7 (overlapped, 3 x C), 25.4, 24.8, 24.7, 24.5, 22.6, 18.3, 18.2, 14.0, -3.8, -4.6, -5.4 (overlapped, 2 x C); MS *m/z*: 763 $[M\text{-}CH_3]^+$, 73 (100%); HRMS (EI) calcd for $C_{36}H_{71}O_4{}^{35}Cl_4Si_2$ $[M\text{-}CH_3]^+$ 763.3645, found: 763.3640.

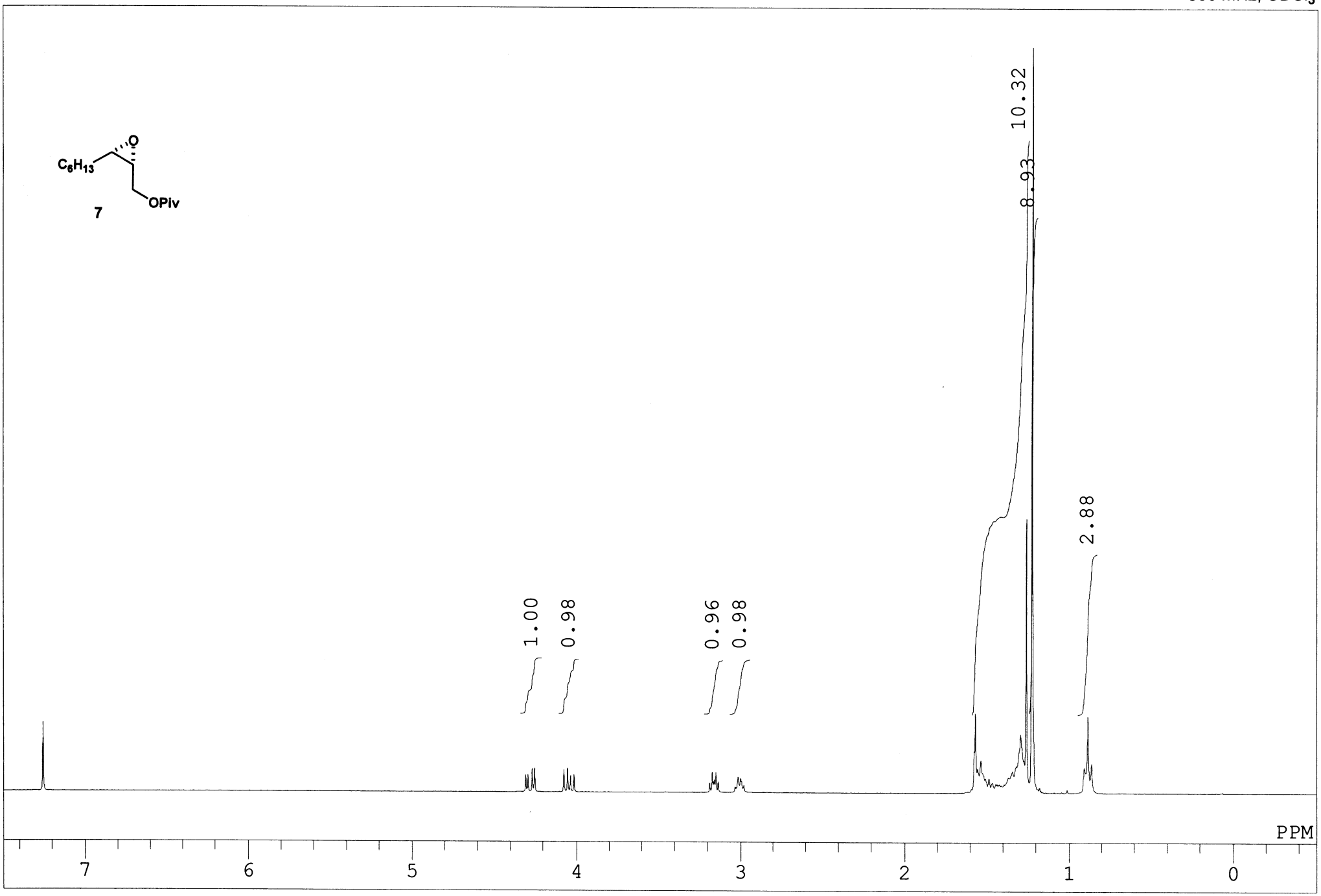


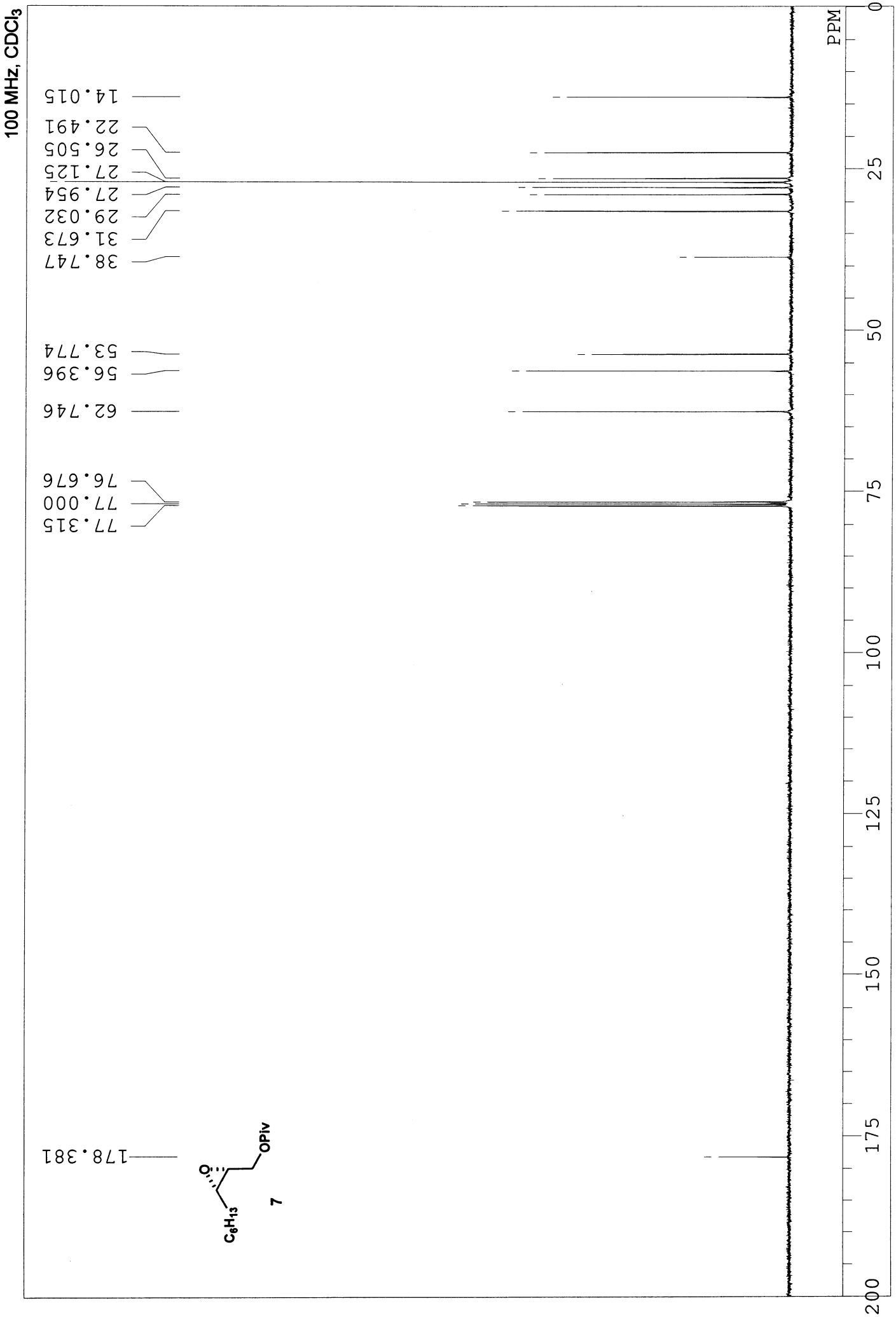
21

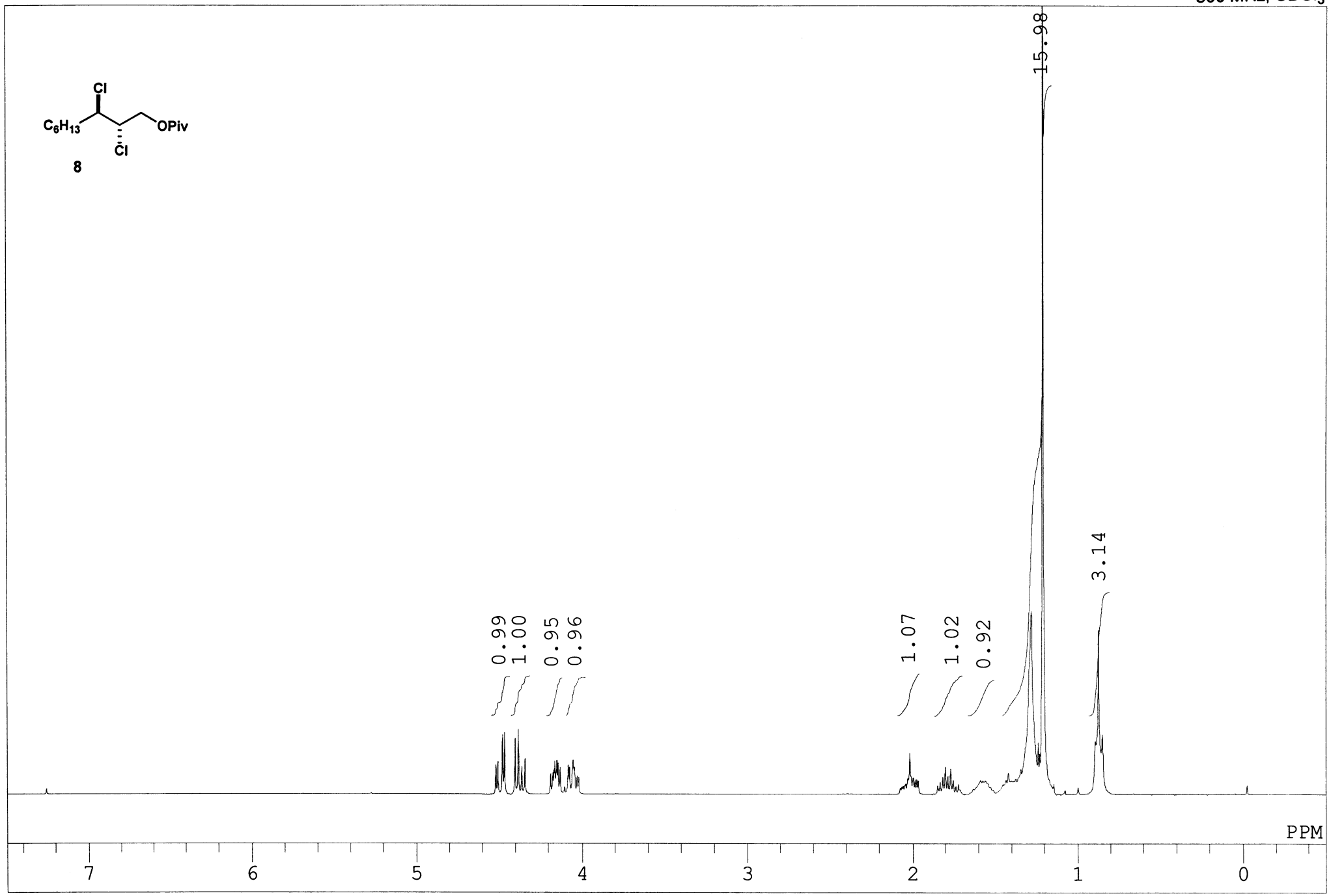
***tert*-Butyl(10-{(4*S*,6*S*)-6-[(1*S*,2*S*,3*R*)-1-(*tert*-butyldimethylsilyloxy)-2,3-dichlorononyl]-2,2-dimethyl-1,3-dioxan-4-yl}-2,2-dichlorodecyloxy)dimethylsilane (21)**: To a stirred solution of *syn*-diol **2** (16.4 mg, 0.022 mmol) in CH_2Cl_2 (1 mL) at room temperature were added 2,2-dimethoxypropane (9.5 μl, 0.077 mmol) and PPTS (2.2 mg, 0.088 mmol). After 45 h, the mixture was poured into a separatory funnel where it was partitioned between CH_2Cl_2 and sat. $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (Et_2O/*n*-hexane 1:50) to give acetal **21** (16.9 mg, 98%) as a pale yellow oil. **Acetal 21**: pale yellow oil; $[\alpha]^{25}{}_D$ +10.3 (*c* 0.82, $CHCl_3$); IR (neat) ν 2955, 2930, 2857, 1462, 1379, 1258, 1202, 1121, 837, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.47 (ddd, 1H, *J* = 10.1, 6.9, 2.7 Hz), 4.24 (ddd, 1H, *J* = 11.4, 5.5, 2.7 Hz), 4.10-4.04 (m, 2H), 3.92 (s, 2H), 3.82 (m, 1H), 2.20-2.14 (m, 2H), 1.99 (m, 1H), 1.75 (m, 1H), 1.65-1.21 (m, 24H), 1.43 (s, 3H), 1.37 (s, 3H), 0.94-0.85 (m, 21H), 0.15 (s, 3H), 0.13 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 98.5, 93.5, 75.3, 72.1, 70.0, 68.9, 68.5, 62.6, 43.5, 36.6, 33.8, 32.0, 31.6, 29.9, 29.5, 29.4, 29.3, 29.0, 28.8, 25.9 (overlapped, 3 x C), 25.72 (overlapped, 3 x C), 25.70, 24.9, 24.7, 22.6, 19.7, 18.3, 18.2, 14.0, -3.7, -4.6, -5.4 (overlapped, 2 x C); MS *m/z*: 763 $[M\text{-}CH_3]^+$, 73 (100%); HRMS (EI) calcd for $C_{36}H_{71}O_4{}^{35}Cl_4Si_2$ $[M\text{-}CH_3]^+$ 763.3645, found: 763.3653.

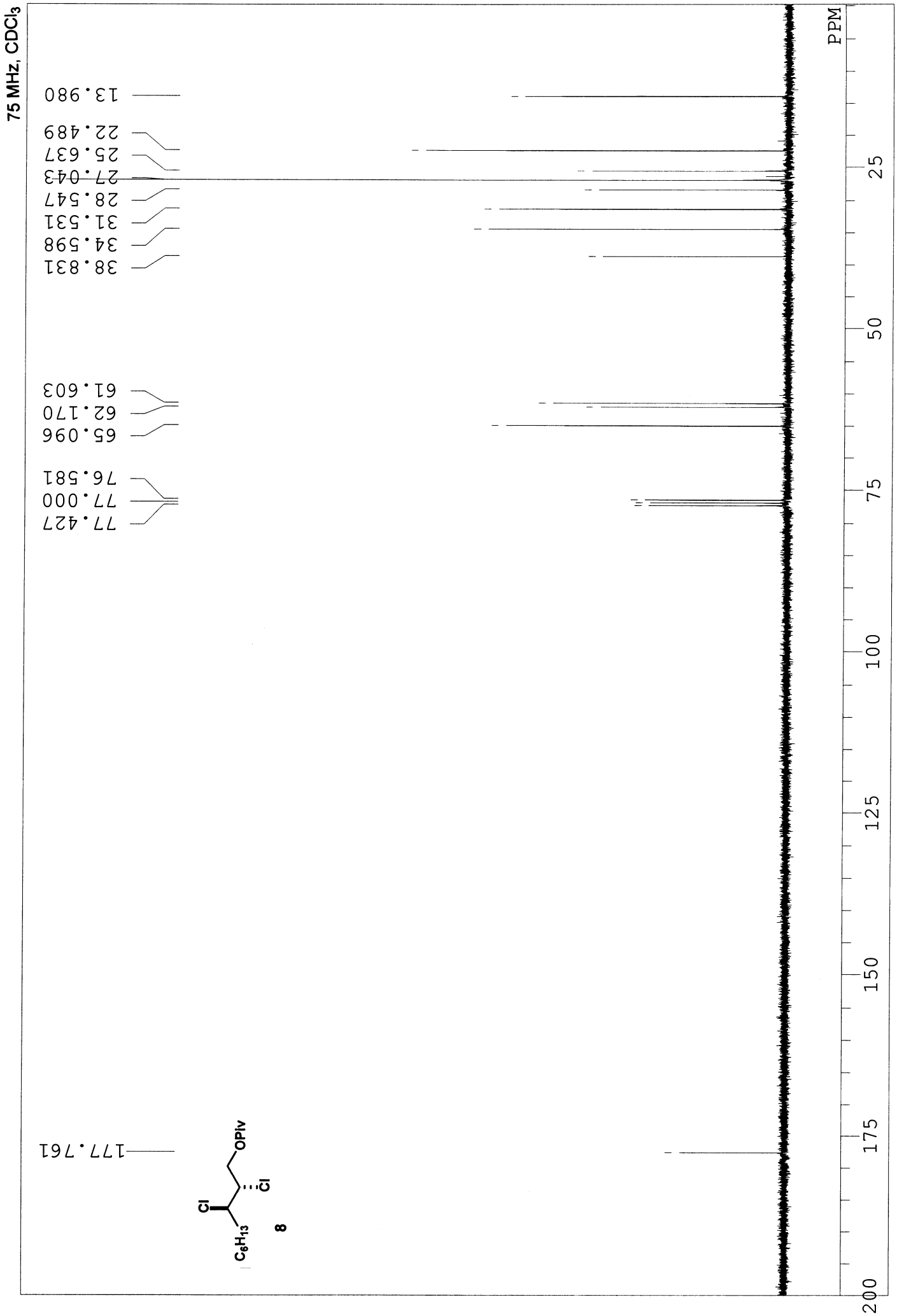
References

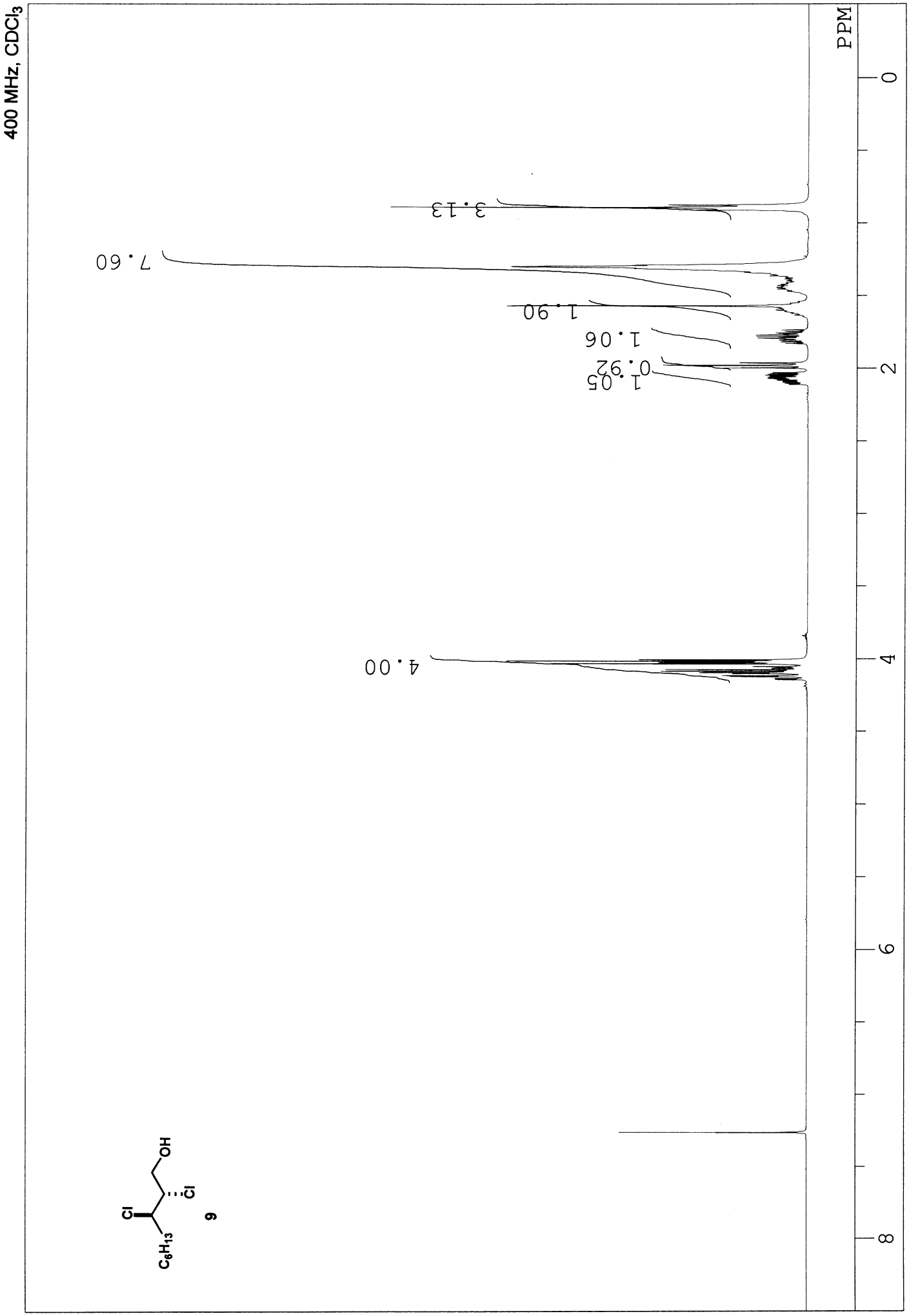
1. (a) Burke, C. P.; Shi, Y. *Org. Lett.* **2009**, *11*, 5150. (b) Kanerva, L. T.; Vänttinen, E. *Tetrahedron. Asymmetry*. **1993**, *4*, 85-90.
2. (a) Kawahara, T.; Kumaki, Y.; Kamada, T.; Ishii, T.; Okino, T. *J. Org. Chem*. **2009**, *74*, 6016-6024. (b) Bedke, D. K.; Shibuya, G. M.; Pereira, A.; Gerwick, W. H.; Haines, T. H.; Vanderwal, C. D. *J. Am. Chem. Soc*. **2009**, *131*, 7570-7572.

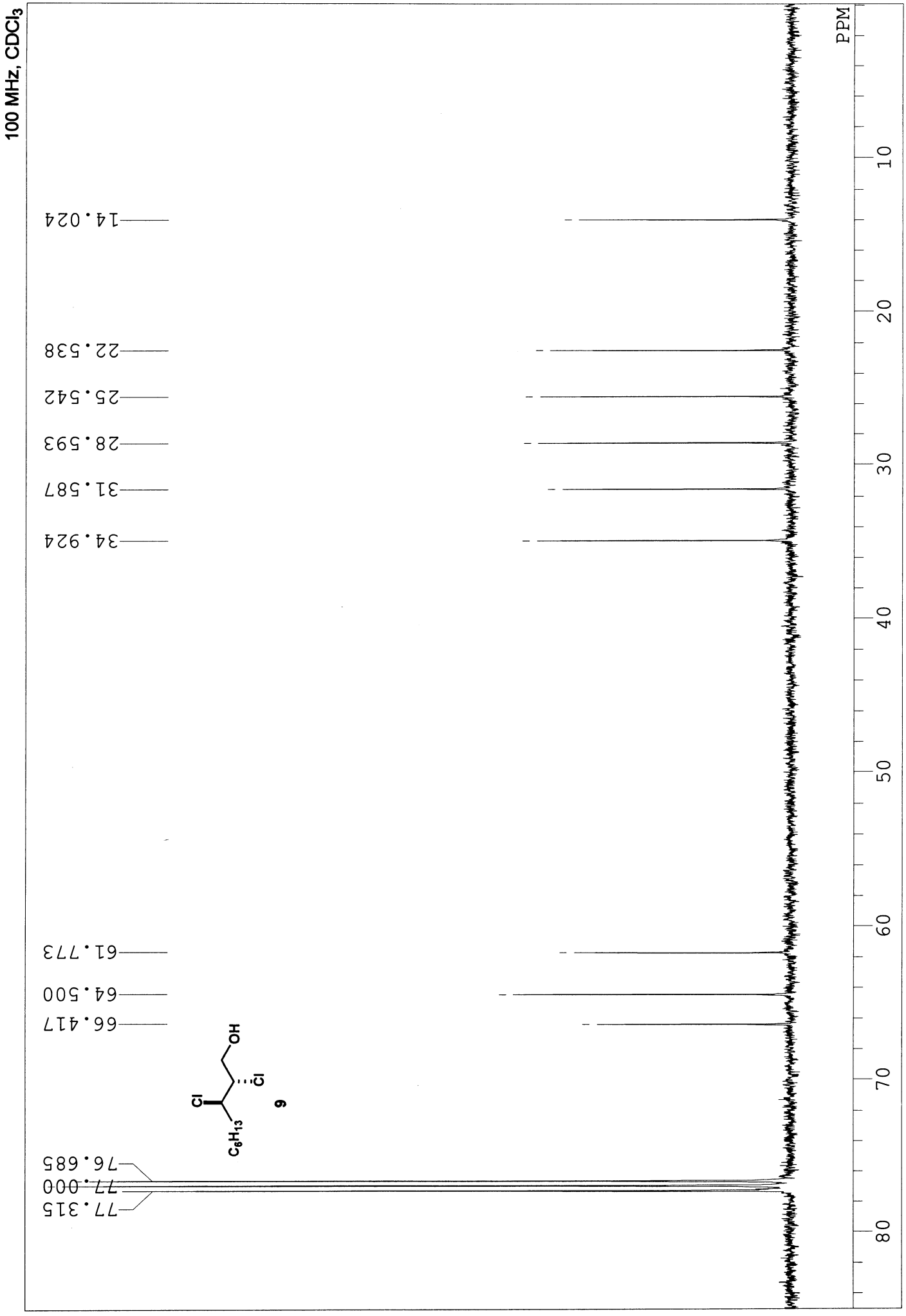

300 MHz, CDCl3
C6H13
O
OPiv
7
10.32
8.93
2.88
1.00
0.98
0.96
0.98
PPM
7
6
5
4
3
2
1
0

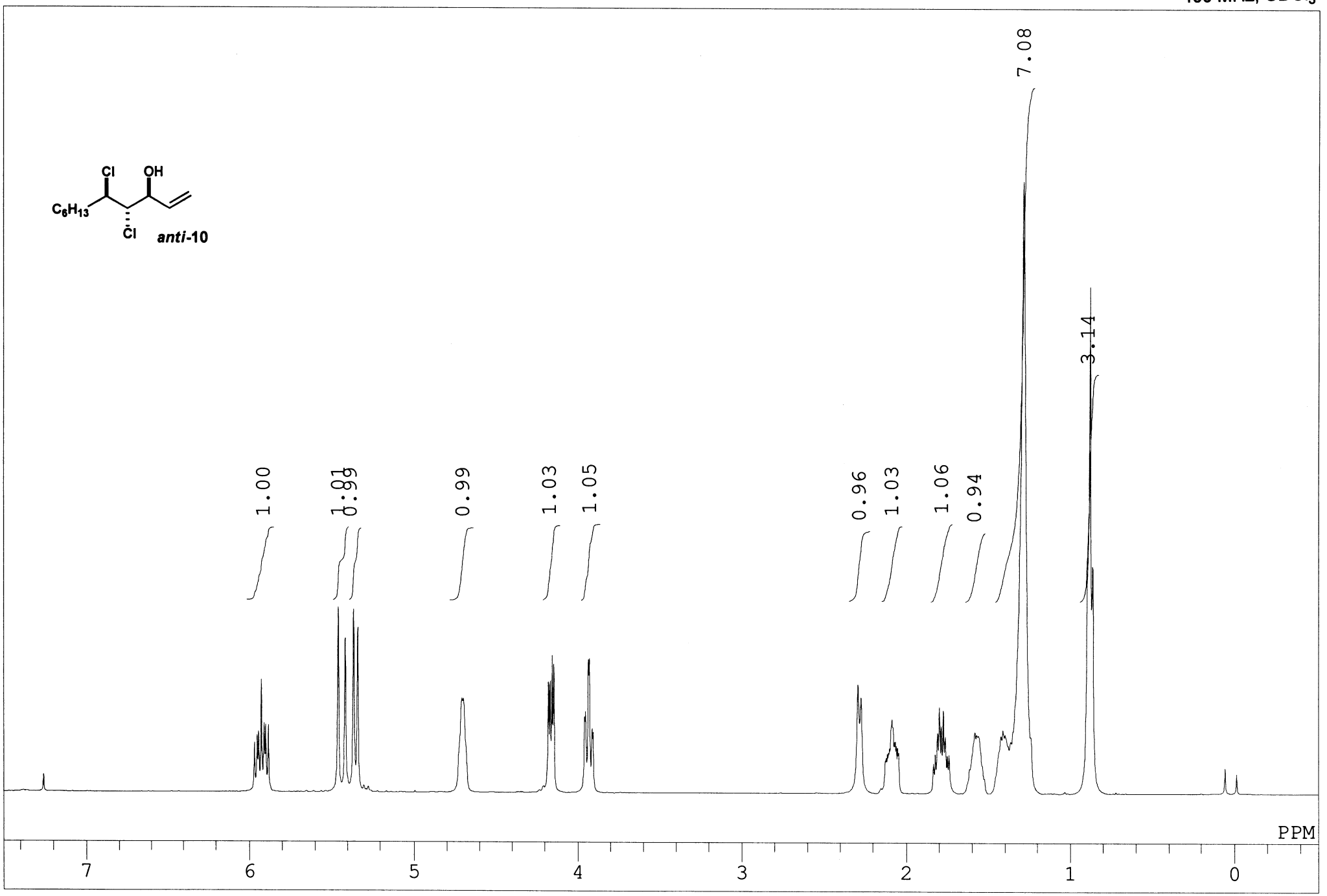

100 MHz, CDCl3
14.015
22.491
26.505
27.125
27.954
29.032
31.673
38.747
53.774
56.396
62.746
76.676
77.000
77.315
178.381
PPM
0
25
50
75
100
125
150
175
200
OPiv
O
C6H13
7


300 MHz, CDCl3
Cl
C6H13
OPiv
Cl
8
15.98
3.14
0.99
1.00
0.95
0.96
1.07
1.02
0.92
PPM
7
6
5
4
3
2
1
0

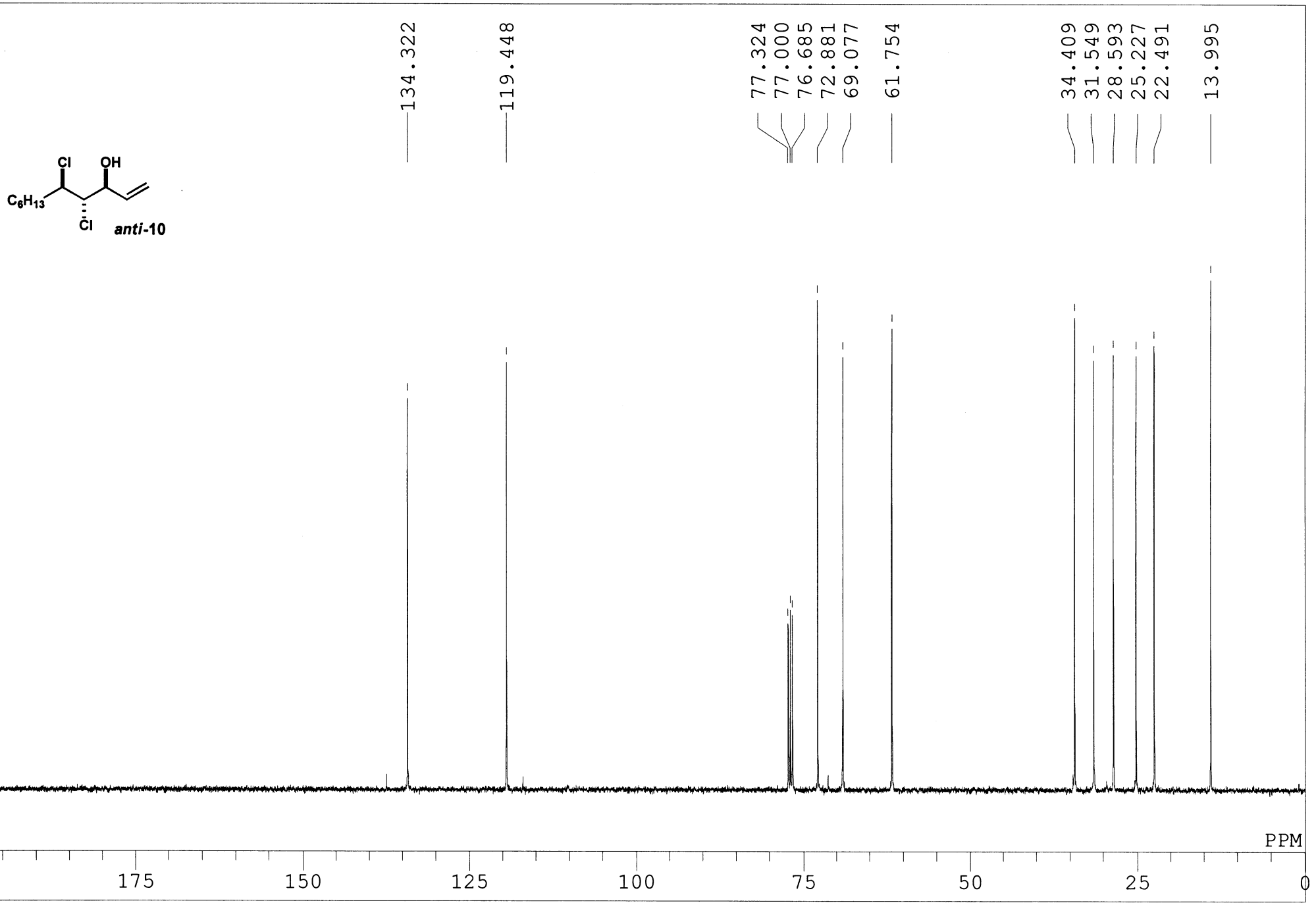

75 MHz, CDCl3
13.980
22.489
25.637
27.043
28.547
31.531
34.598
38.831
61.603
62.170
65.096
76.581
77.000
77.427
177.761
PPM
25
50
75
100
125
150
175
200
OPiv
Cl
Cl
C6H13
8


400 MHz, CDCl3
PPM
0
2
4
6
8
4.00
1.05
0.92
1.06
1.90
7.60
3.13
OH
Cl
Cl
C6H13
9

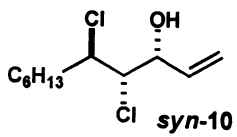

100 MHz, CDCl3
PPM
10
20
30
40
50
60
70
80
14.024
22.538
25.542
28.593
31.587
34.924
61.773
64.500
66.417
76.685
77.000
77.315
OH
Cl
Cl
C6H13
9


400 MHz, CDCl3
Cl
OH
C6H13
Cl
anti-10
1.00
1.01
0.99
1.03
1.05
0.96
1.03
1.06
0.94
7.08
3.14
PPM
7
6
5
4
3
2
1
0

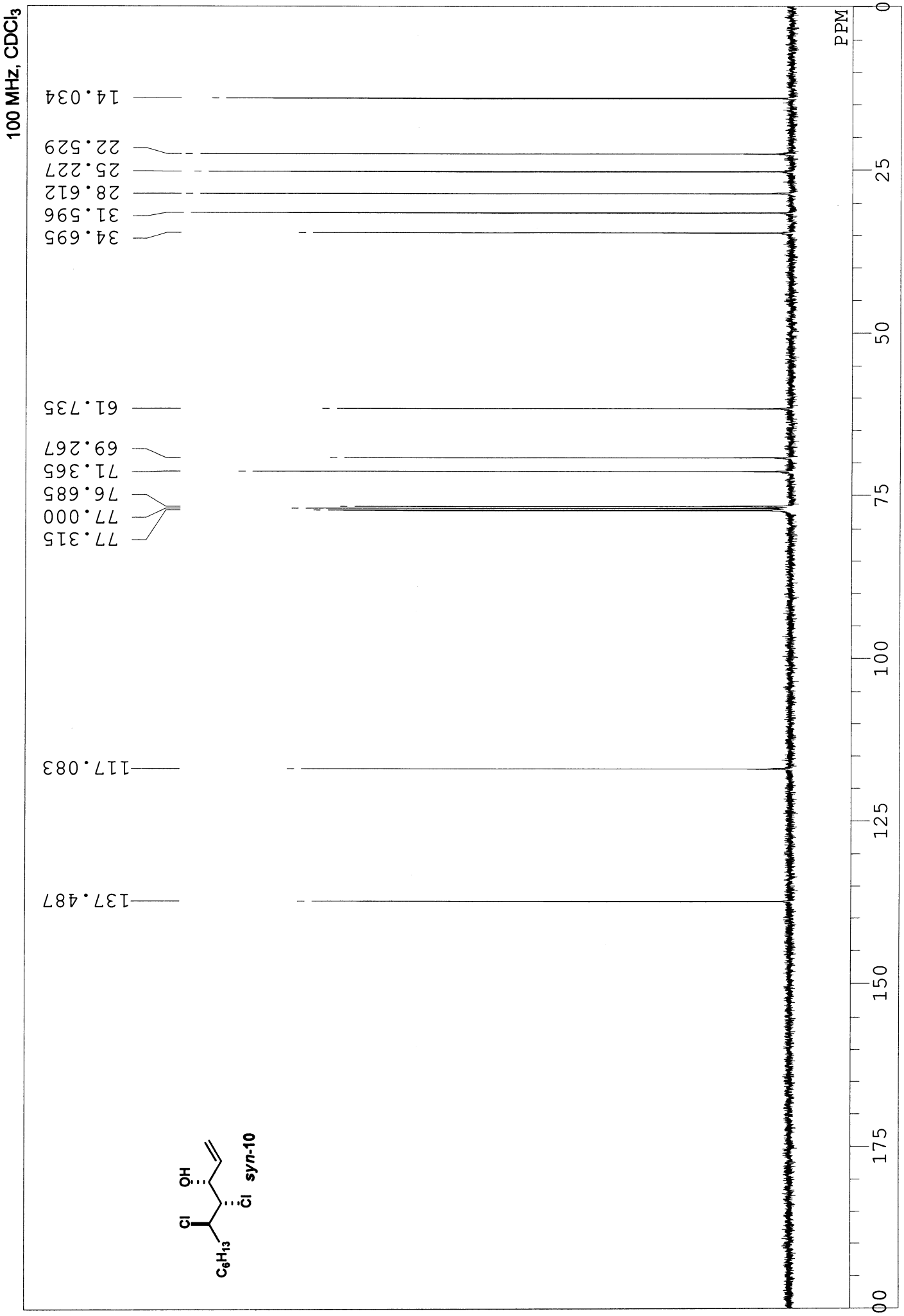
100 MHz, $CDCl_3$

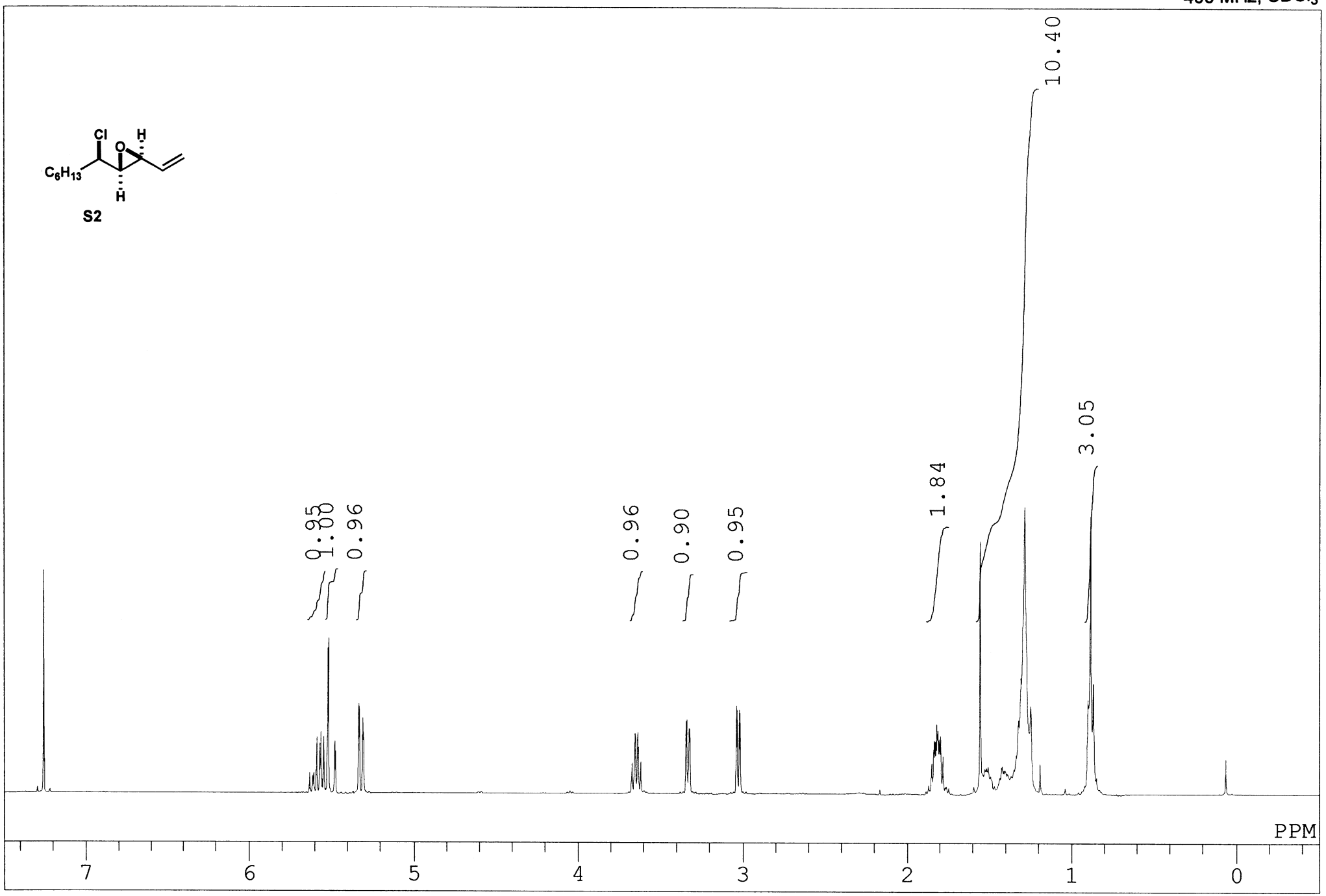


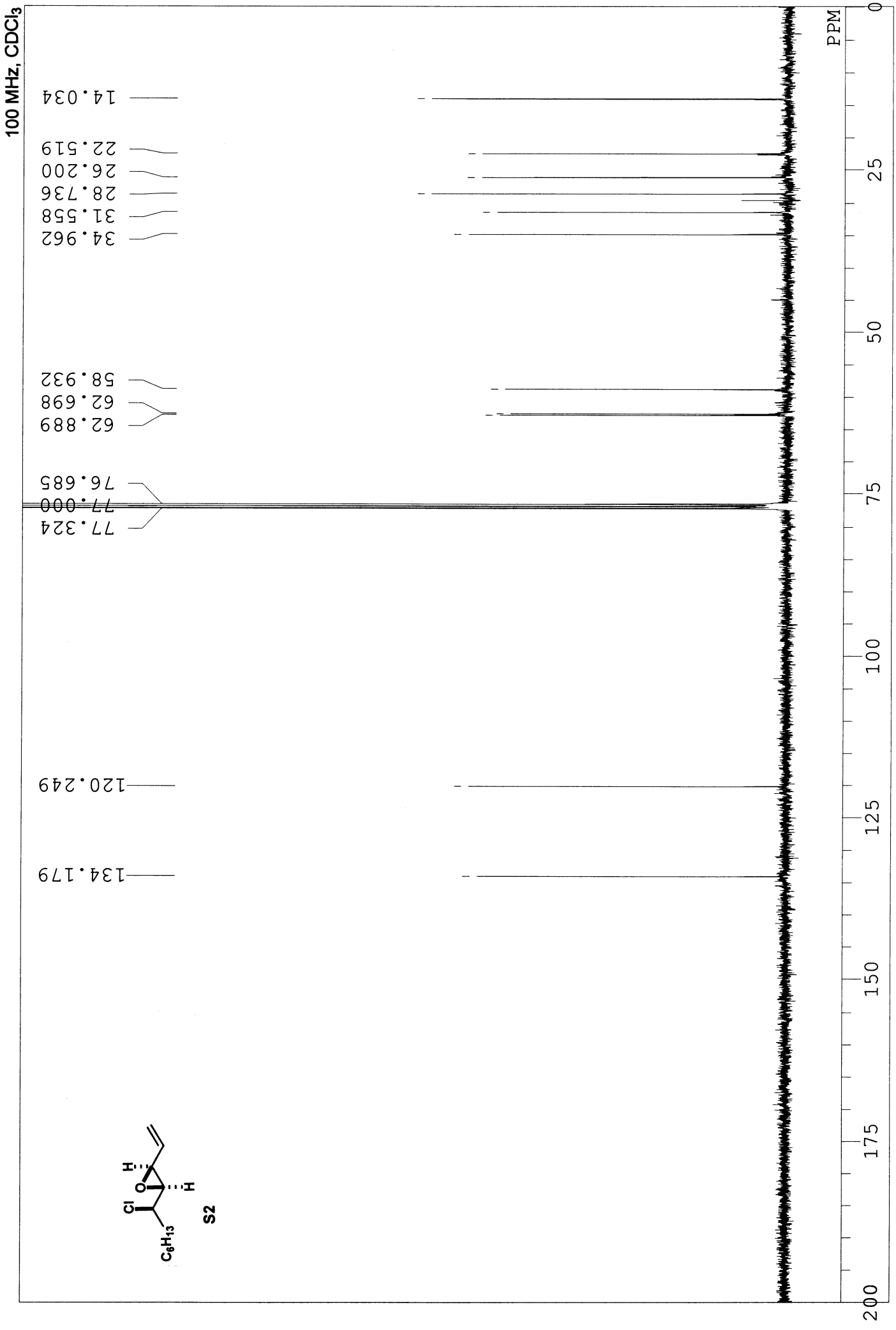
400 MHz, $CDCl_3$

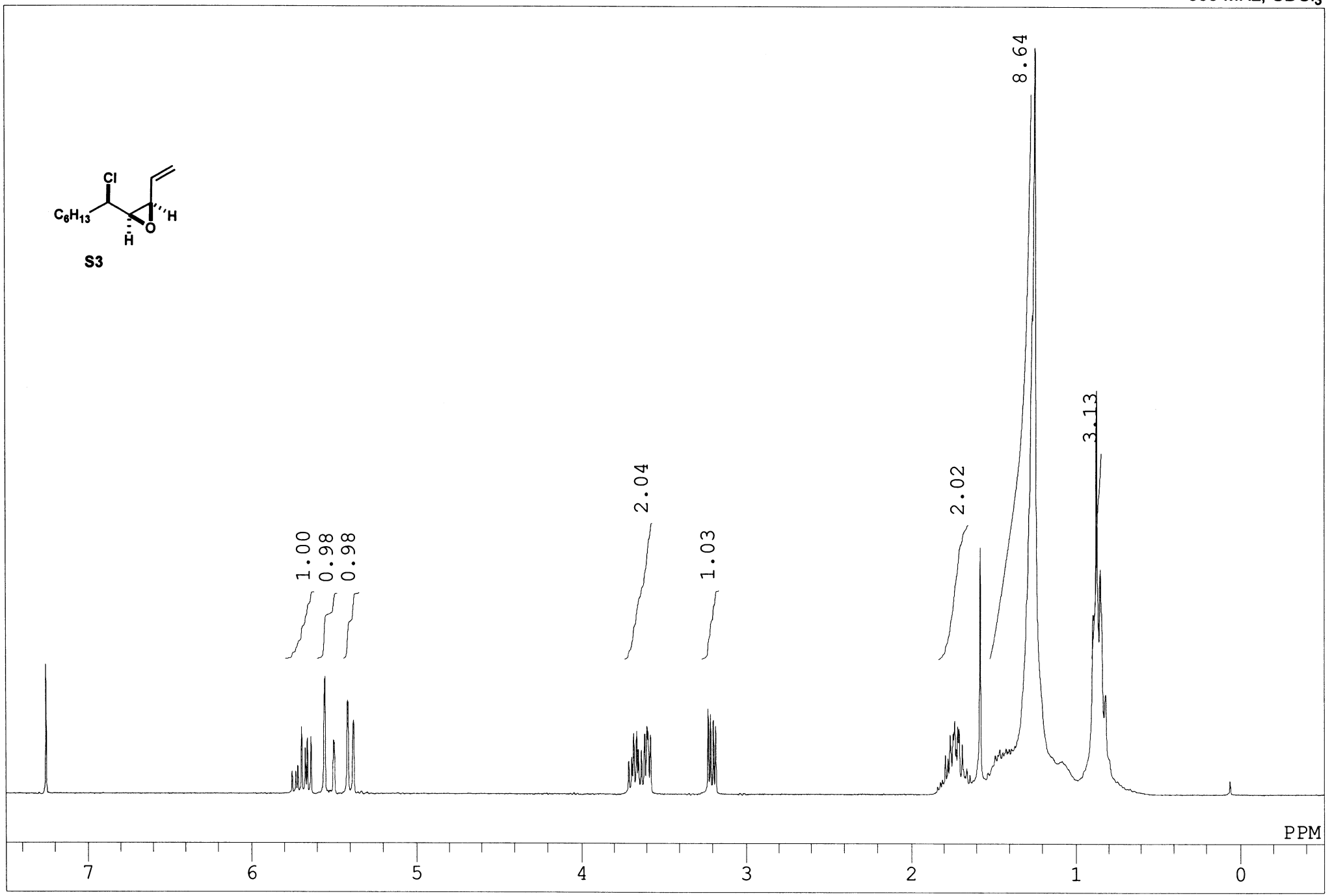


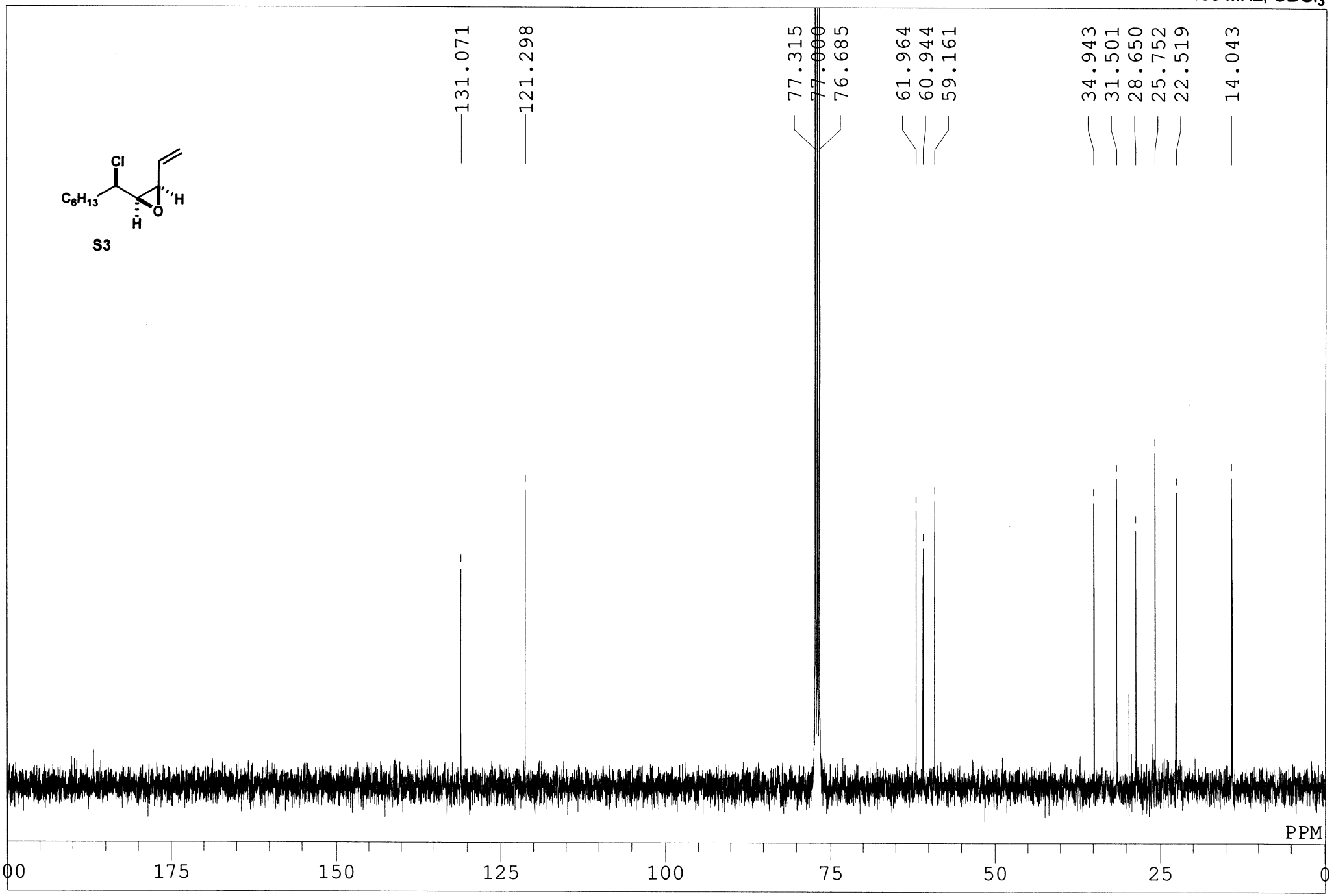
syn-10

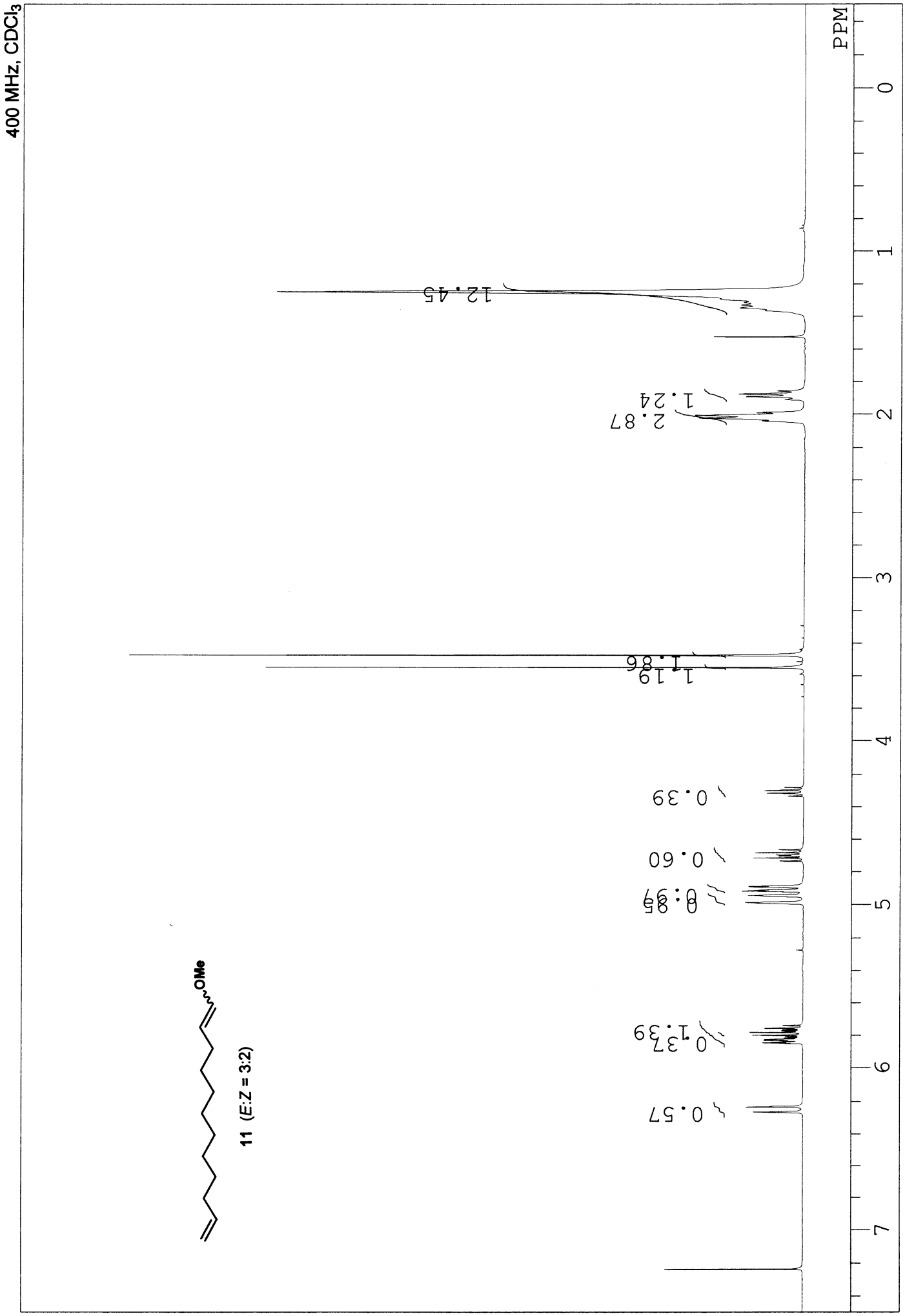

100 MHz, CDCl3
14.034
22.529
25.227
28.612
31.596
34.695
61.735
69.267
71.365
76.685
77.000
77.315
117.083
137.487
PPM
0
25
50
75
100
125
150
175
200
OH
Cl
Cl
C6H13
syn-10

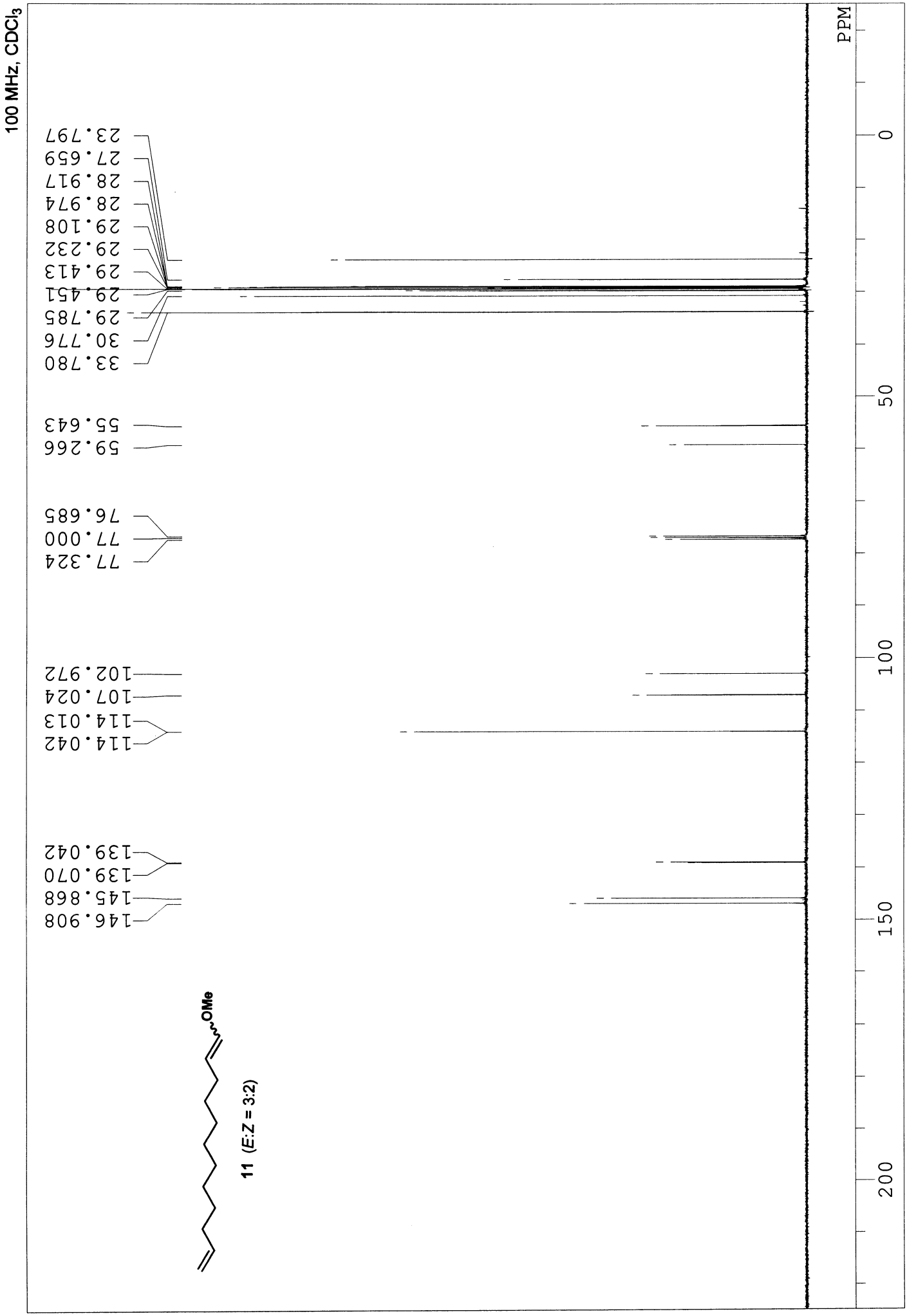

400 MHz, CDCl3
Cl
H
O
C6H13
H
S2
10.40
3.05
1.84
0.96
0.90
0.95
1.00
0.96
PPM
7
6
5
4
3
2
1
0


100 MHz, CDCl3
14.034
22.519
26.200
28.736
31.558
34.962
58.932
62.698
62.889
76.685
77.000
77.324
120.249
134.179
PPM
0
25
50
75
100
125
150
175
200
H
O
H
Cl
C6H13
S2

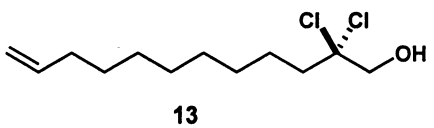

300 MHz, CDCl3
Cl
C6H13
H
O
H
S3
1.00
0.98
0.98
2.04
1.03
2.02
8.64
3.13
PPM
7
6
5
4
3
2
1
0


100 MHz, CDCl3
131.071
121.298
77.315
77.000
76.685
61.964
60.944
59.161
34.943
31.501
28.650
25.752
22.519
14.043
Cl
C6H13
O
H
H
S3
PPM
200
175
150
125
100
75
50
25
0

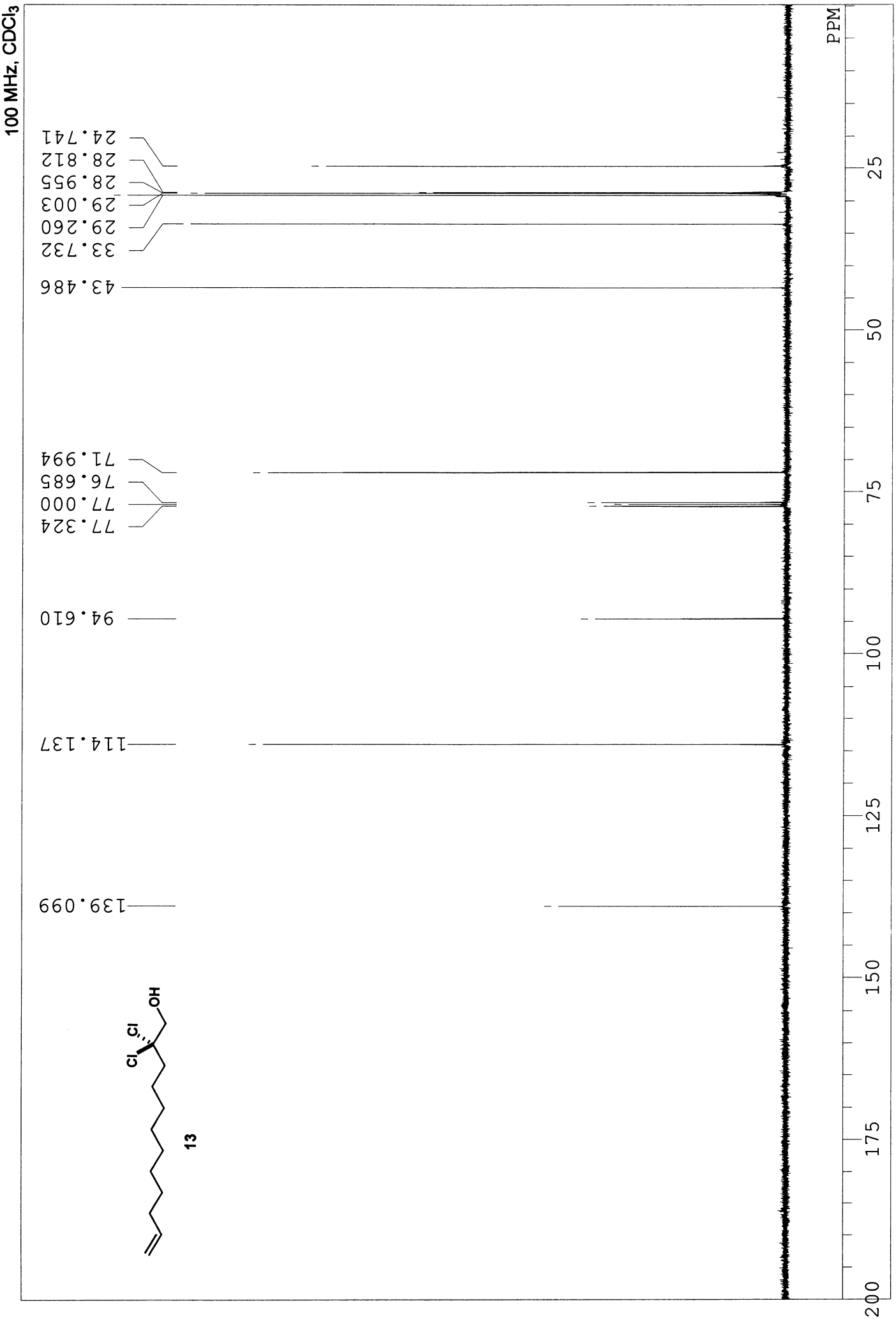

400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
12.45
2.87
1.24
1.19
1.86
0.39
0.60
0.85
0.99
1.37
1.39
0.57
OMe
11 (E:Z = 3:2)

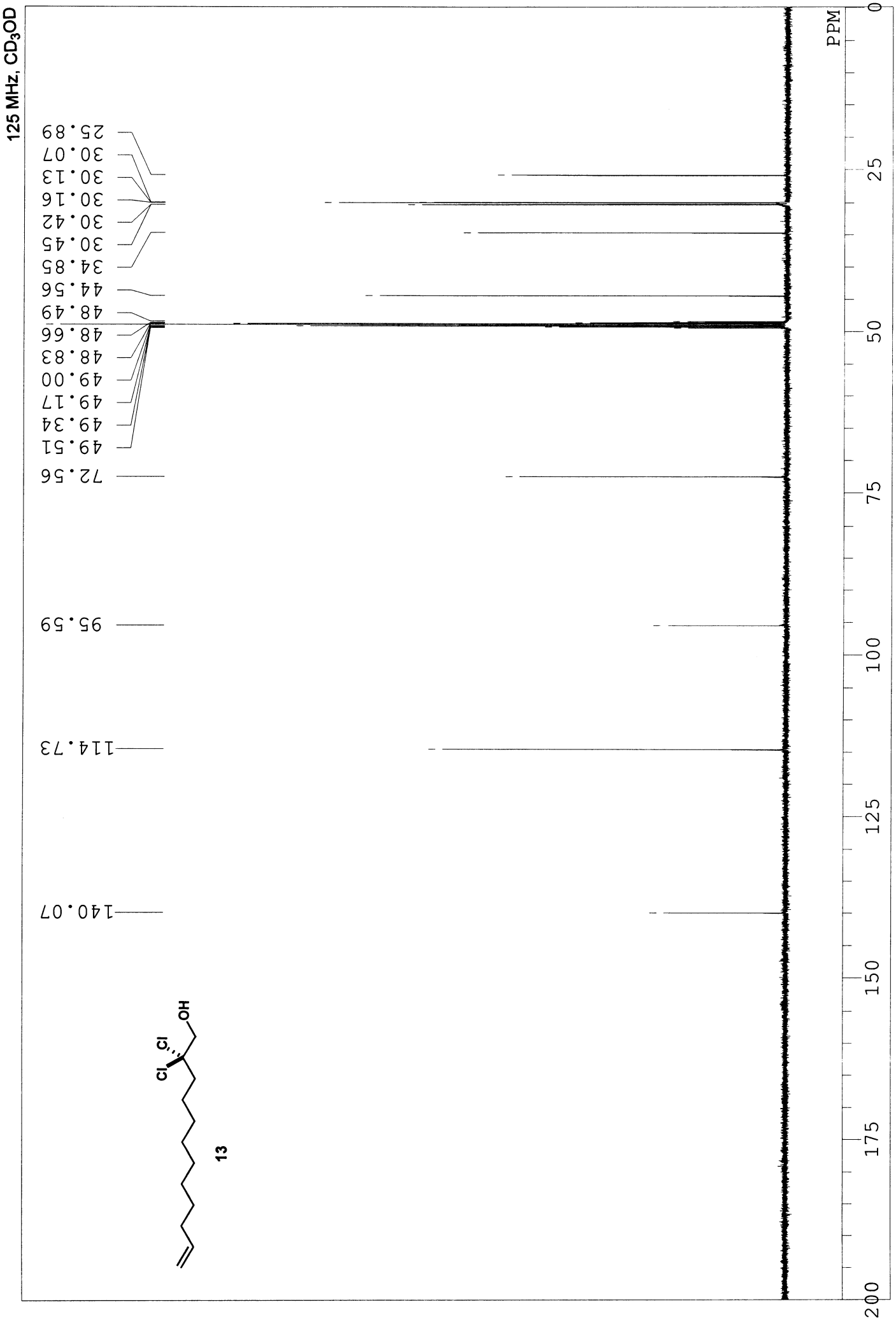

100 MHz, CDCl3
PPM
0
50
100
150
200
23.797
27.659
28.917
28.974
29.108
29.232
29.413
29.451
29.785
30.776
33.780
55.643
59.266
76.685
77.000
77.324
102.972
107.024
114.013
114.042
139.042
139.070
145.868
146.908
OMe
11 (E:Z = 3:2)

400 MHz, $CDCl_3$

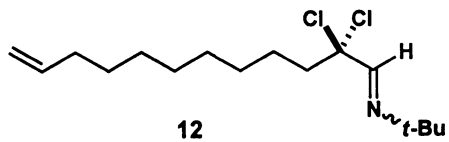


13

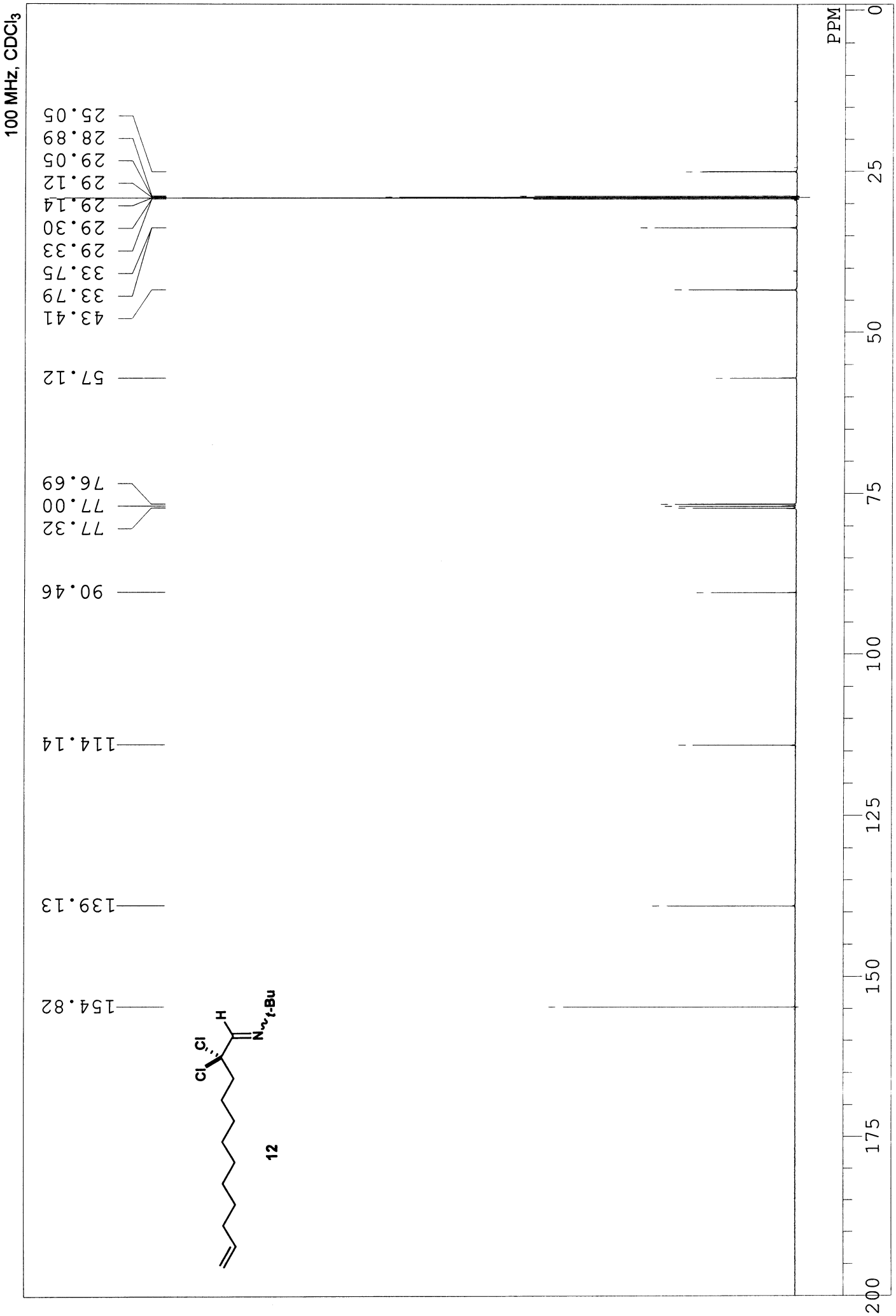

100 MHz, CDCl3
24.741
28.812
28.955
29.003
29.260
33.732
43.486
71.994
76.685
77.000
77.324
94.610
114.137
139.099
PPM
25
50
75
100
125
150
175
200
OH
Cl
Cl
13

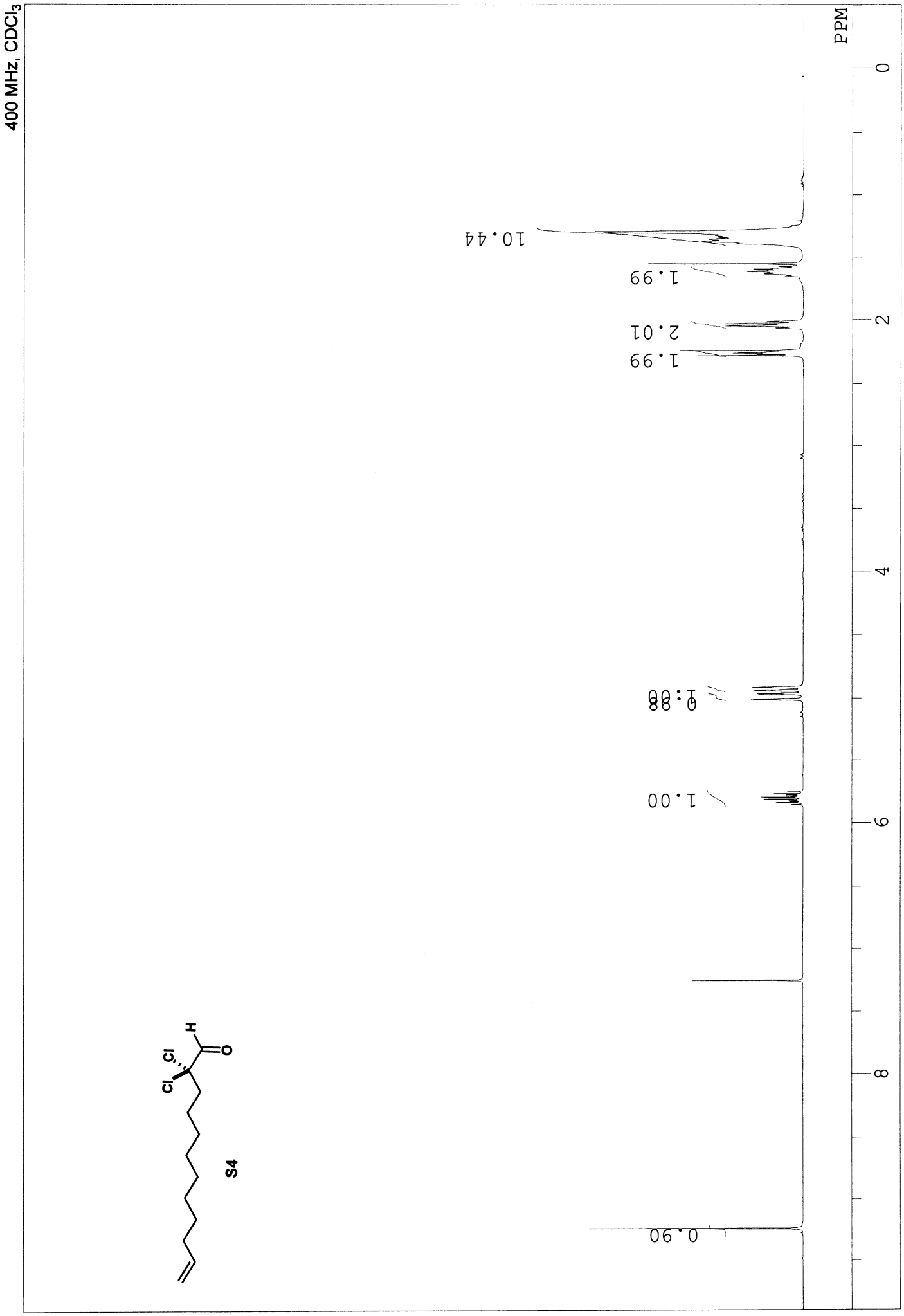

125 MHz, CD3OD
PPM
0
25
50
75
100
125
150
175
200
25.89
30.07
30.13
30.16
30.42
30.45
34.85
44.56
48.49
48.66
48.83
49.00
49.17
49.34
49.51
72.56
95.59
114.73
140.07
OH
Cl
Cl
13

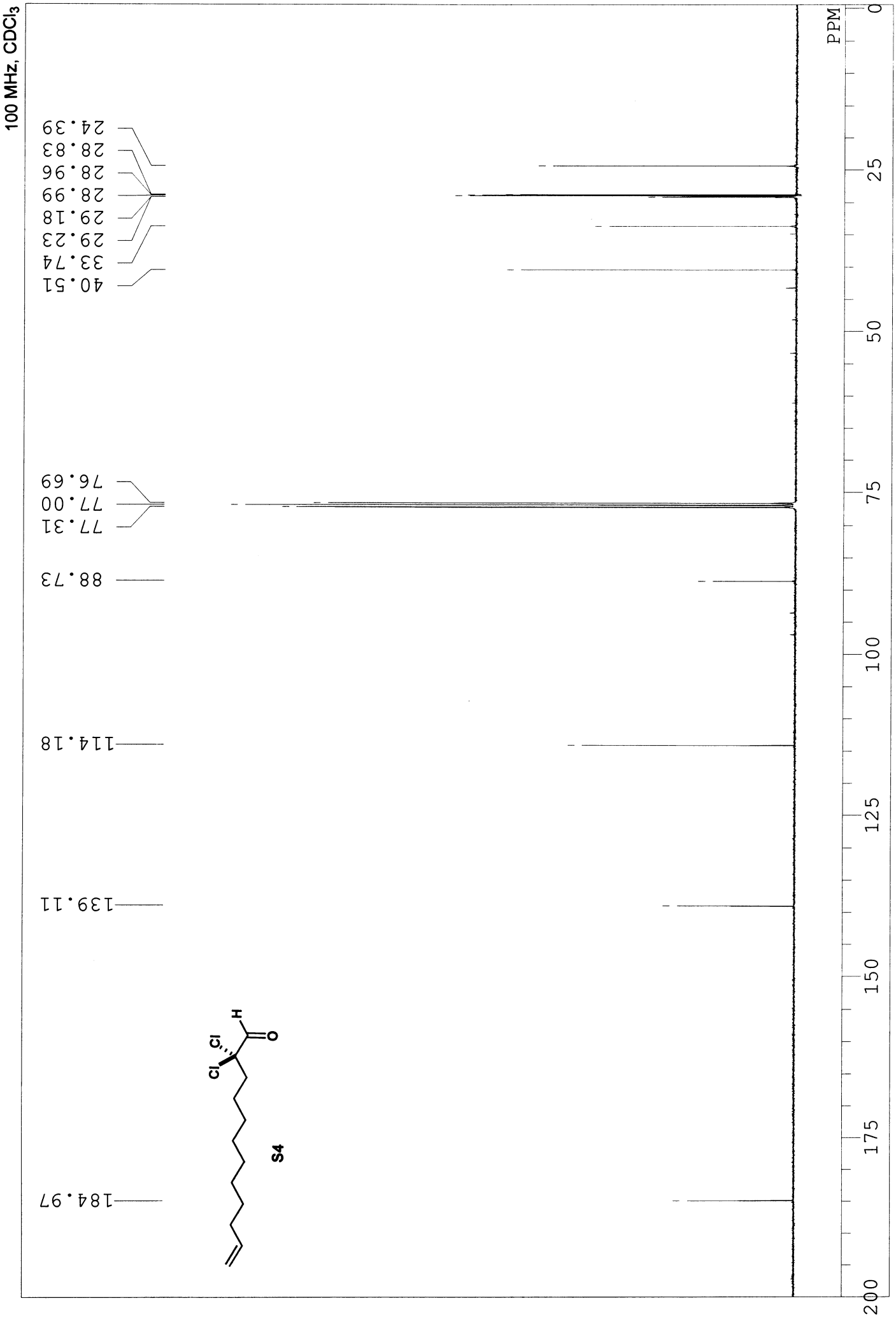
400 MHz, $CDCl_3$

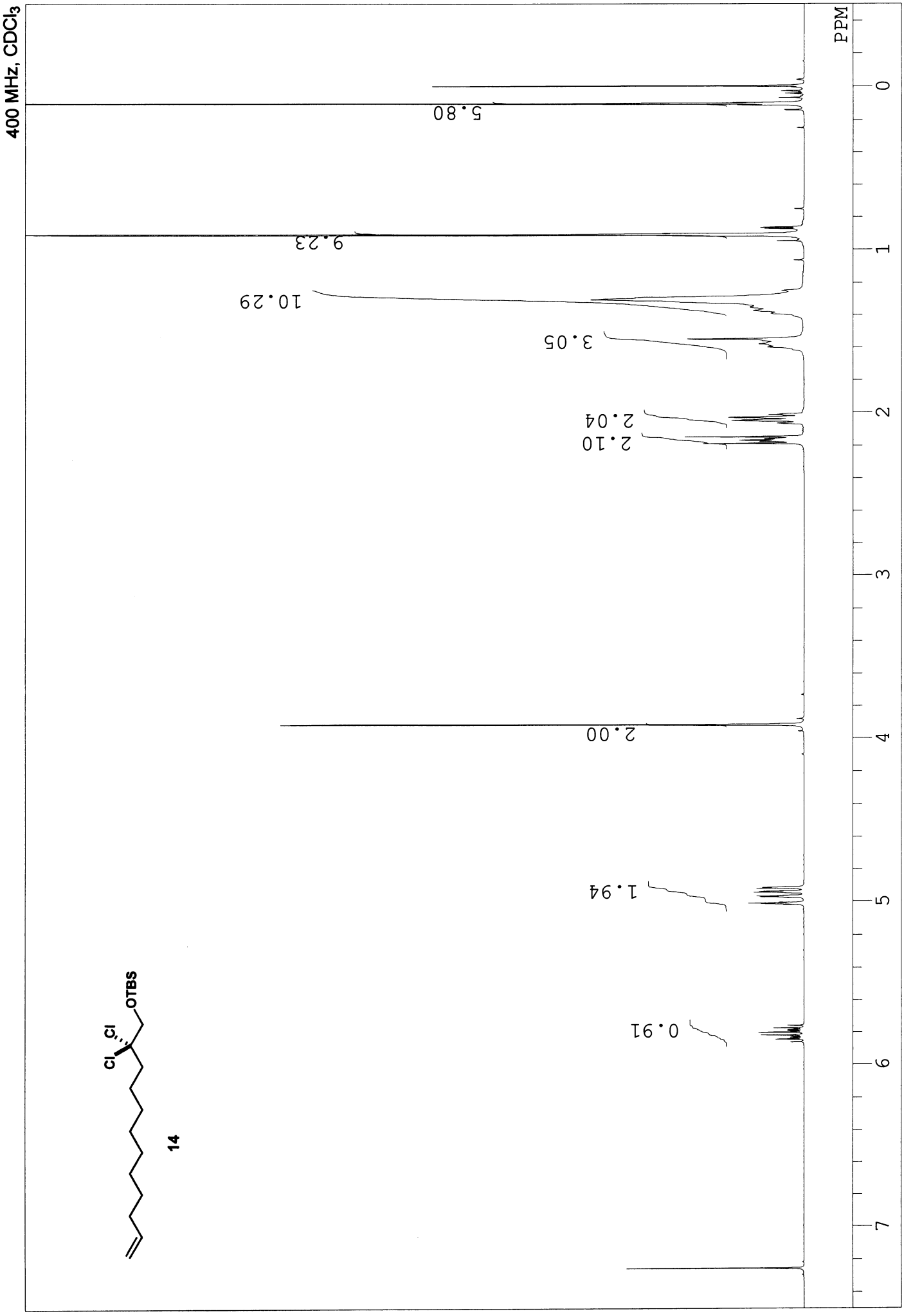


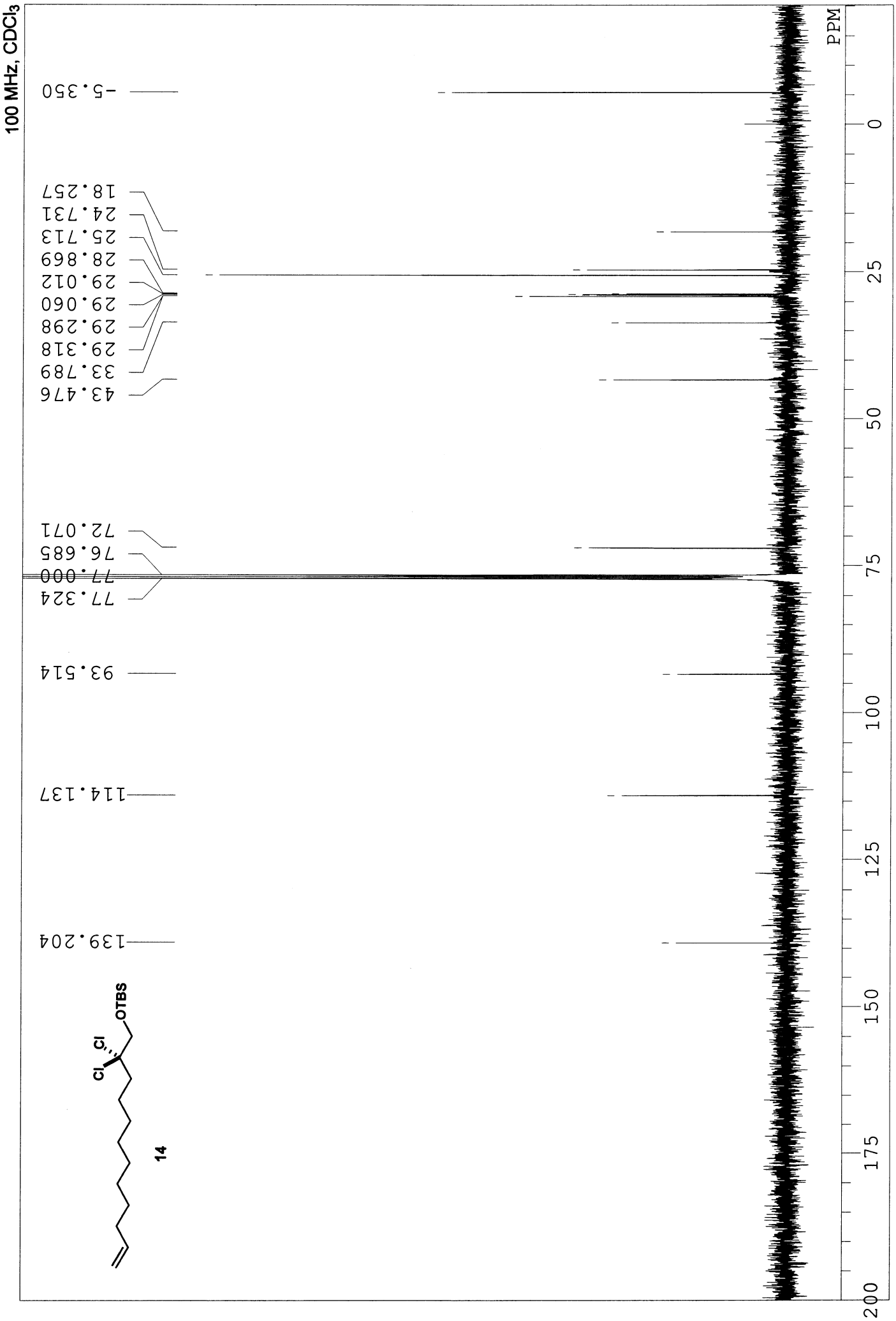
12

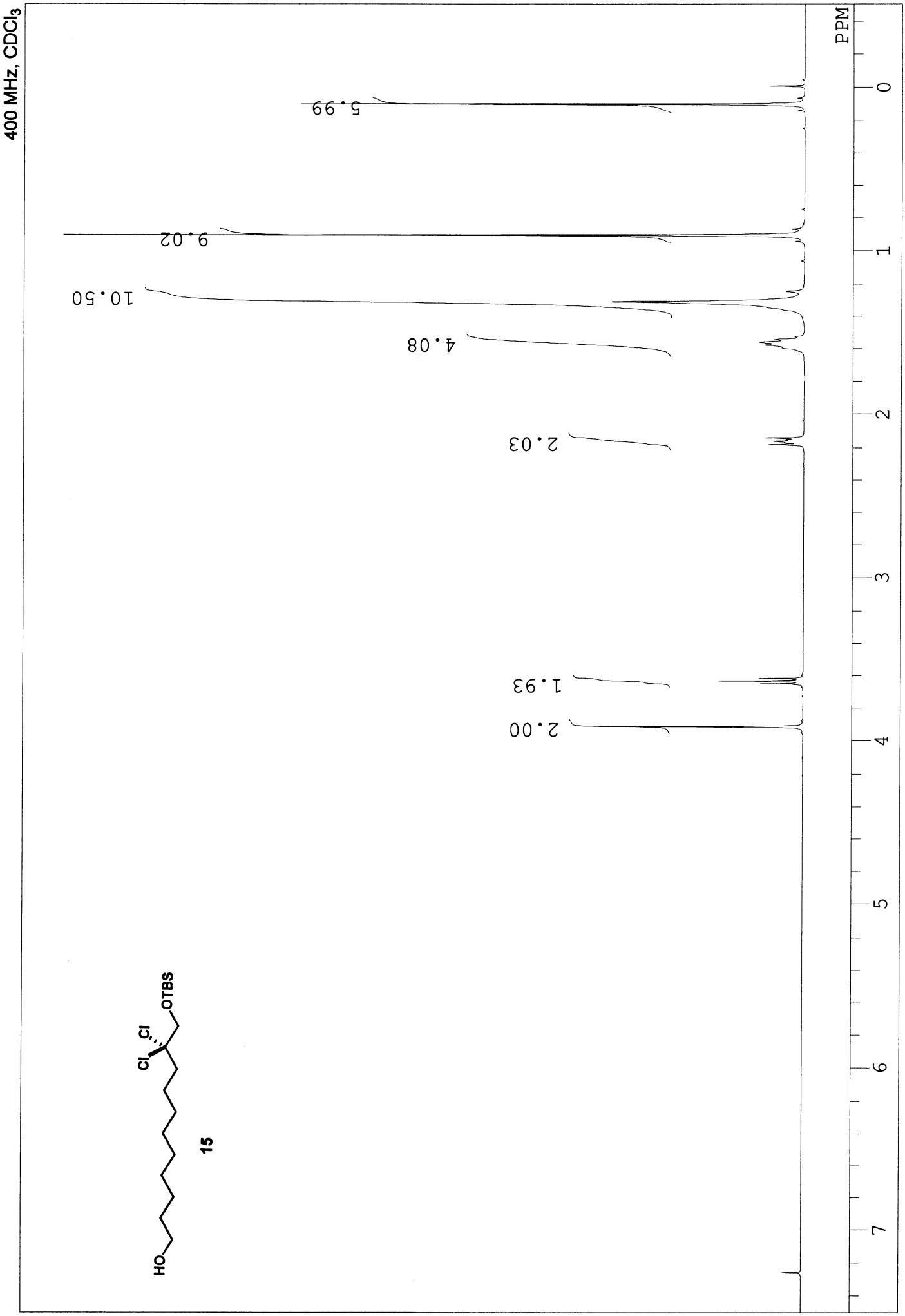

100 MHz, CDCl3
25.05
28.89
29.05
29.12
29.14
29.30
29.33
33.75
33.79
43.41
57.12
76.69
77.00
77.32
90.46
114.14
139.13
154.82
PPM
0
25
50
75
100
125
150
175
200
Cl
Cl
H
N
t-Bu
12

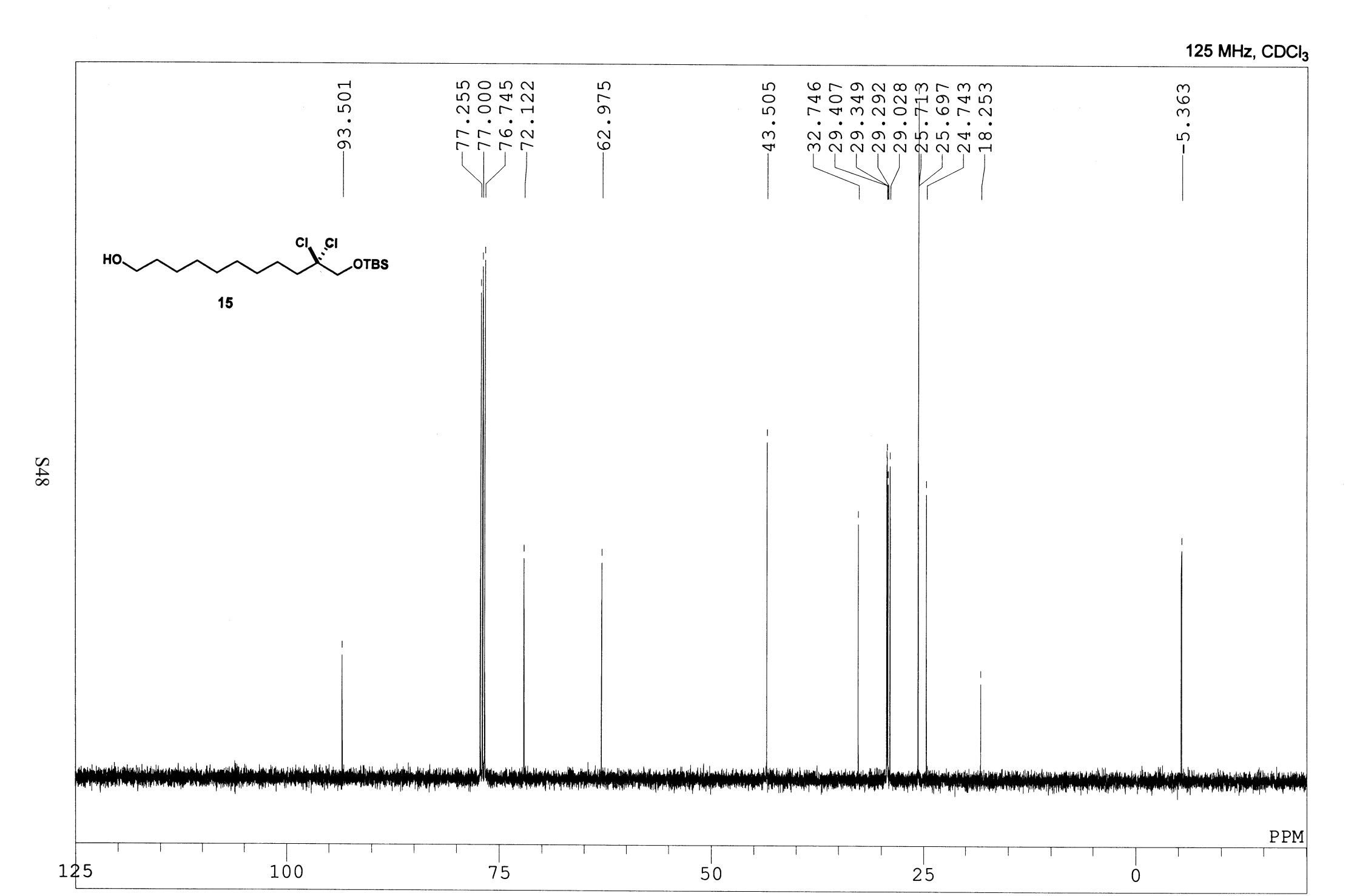

400 MHz, CDCl3
PPM
0
2
4
6
8
10.44
1.99
2.01
1.99
0.88
1.00
0.90
Cl
Cl
H
O
S4

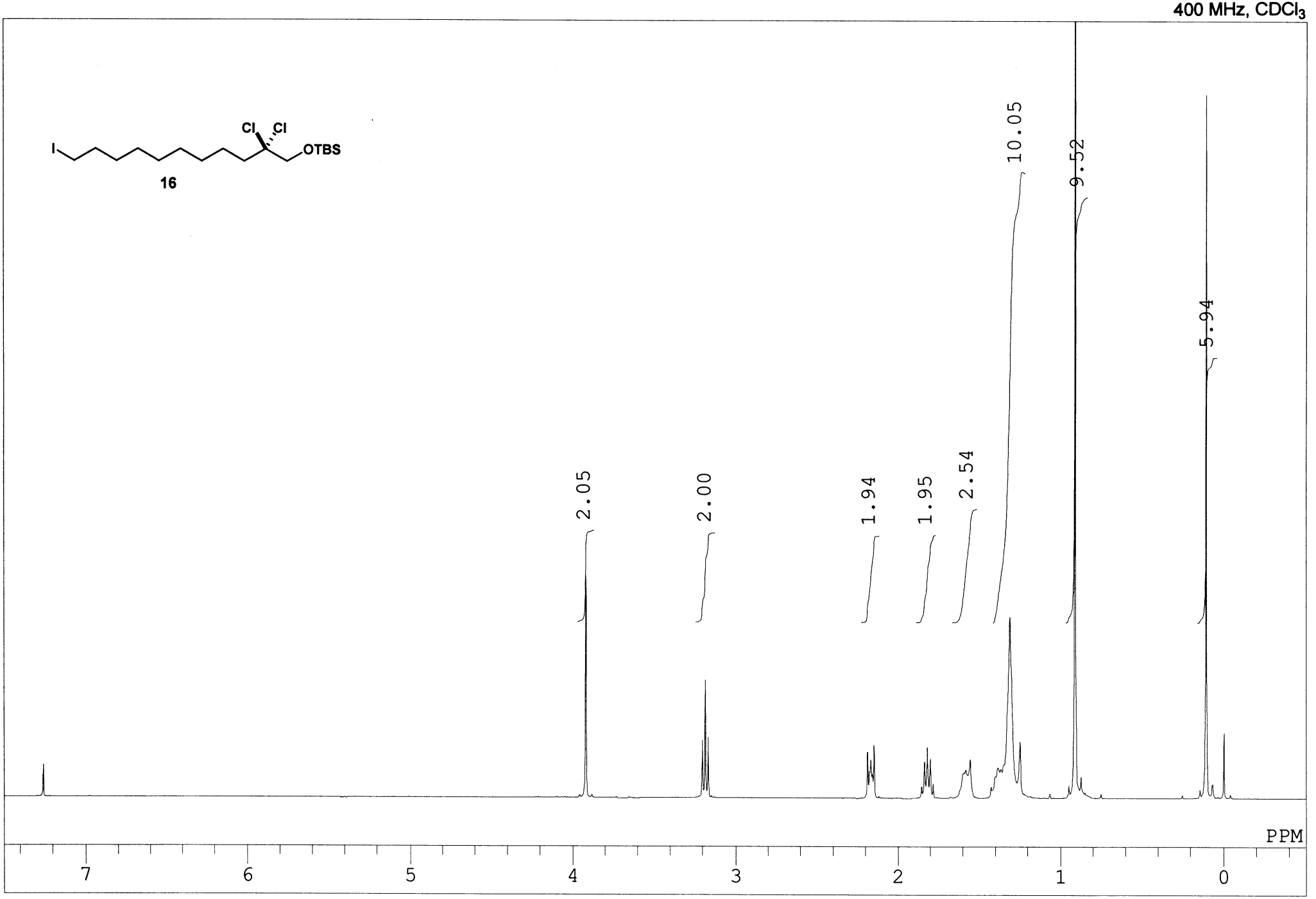

100 MHz, CDCl3
PPM
0
25
50
75
100
125
150
175
200
24.39
28.83
28.96
28.99
29.18
29.23
33.74
40.51
76.69
77.00
77.31
88.73
114.18
139.11
184.97
Cl
Cl
H
O
S4


400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
5.80
9.23
10.29
3.05
2.04
2.10
2.00
1.94
0.91
Cl
Cl
OTBS
14

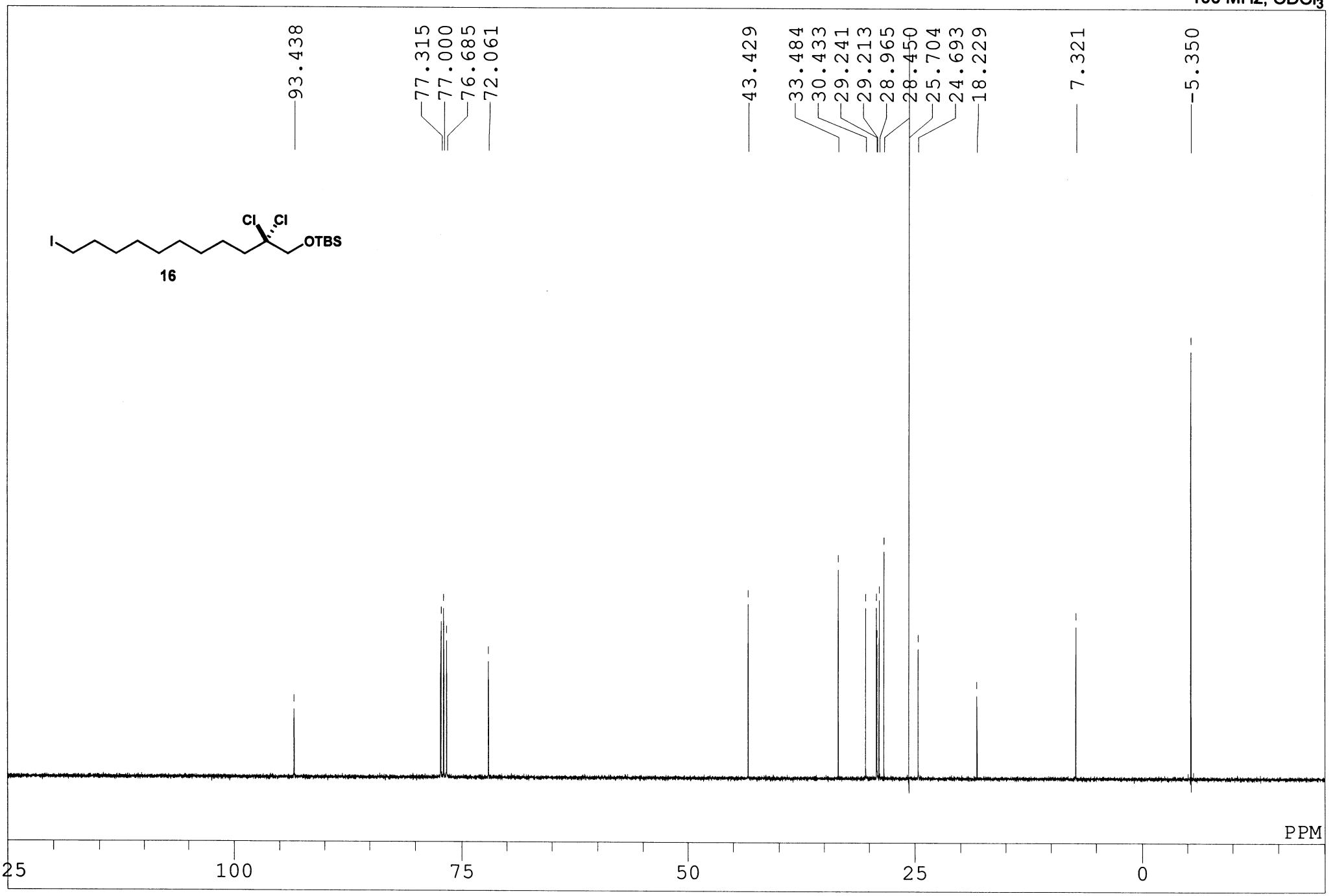

100 MHz, CDCl3
-5.350
18.257
24.731
25.713
28.869
29.012
29.060
29.298
29.318
33.789
43.476
72.071
76.685
77.000
77.324
93.514
114.137
139.204
PPM
0
25
50
75
100
125
150
175
200
OTBS
Cl
Cl
14

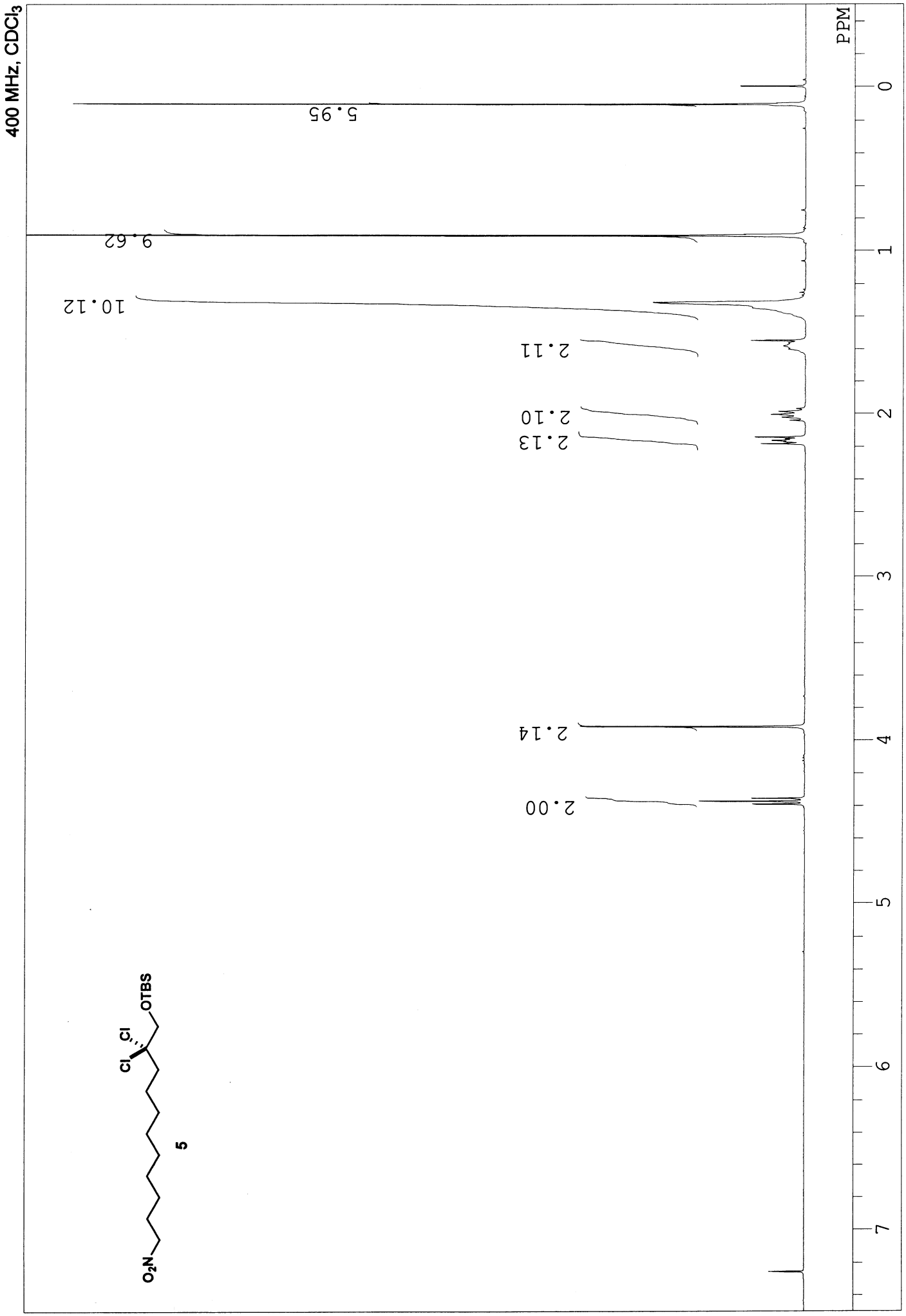

400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
5.99
9.02
10.50
4.08
2.03
1.93
2.00
OTBS
Cl
Cl
HO
15

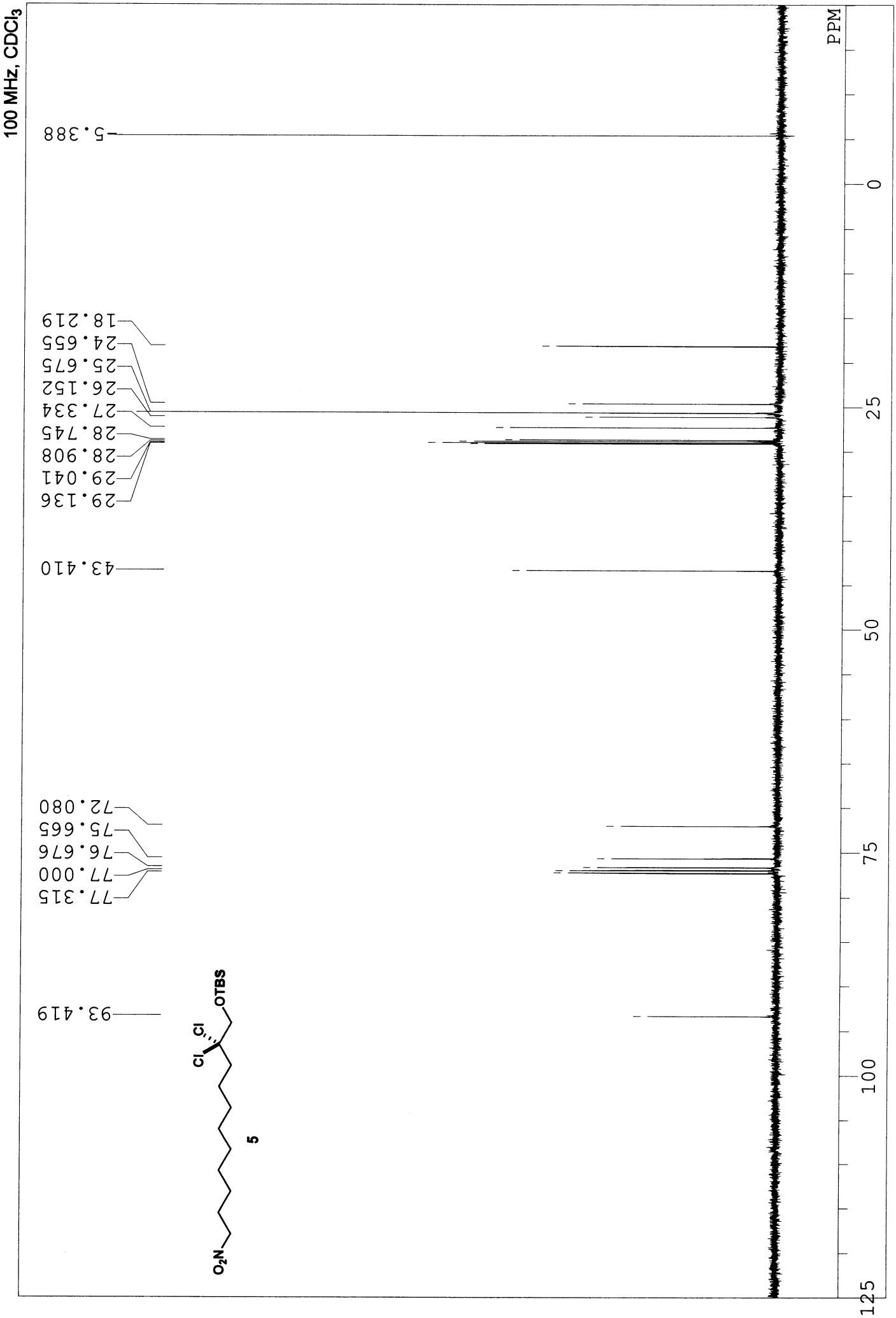

125 MHz, CDCl3
93.501
77.255
77.000
76.745
72.122
62.975
43.505
32.746
29.407
29.349
29.292
29.028
25.713
25.697
24.743
18.253
-5.363
HO
Cl
Cl
OTBS
15
PPM
125
100
75
50
25
0

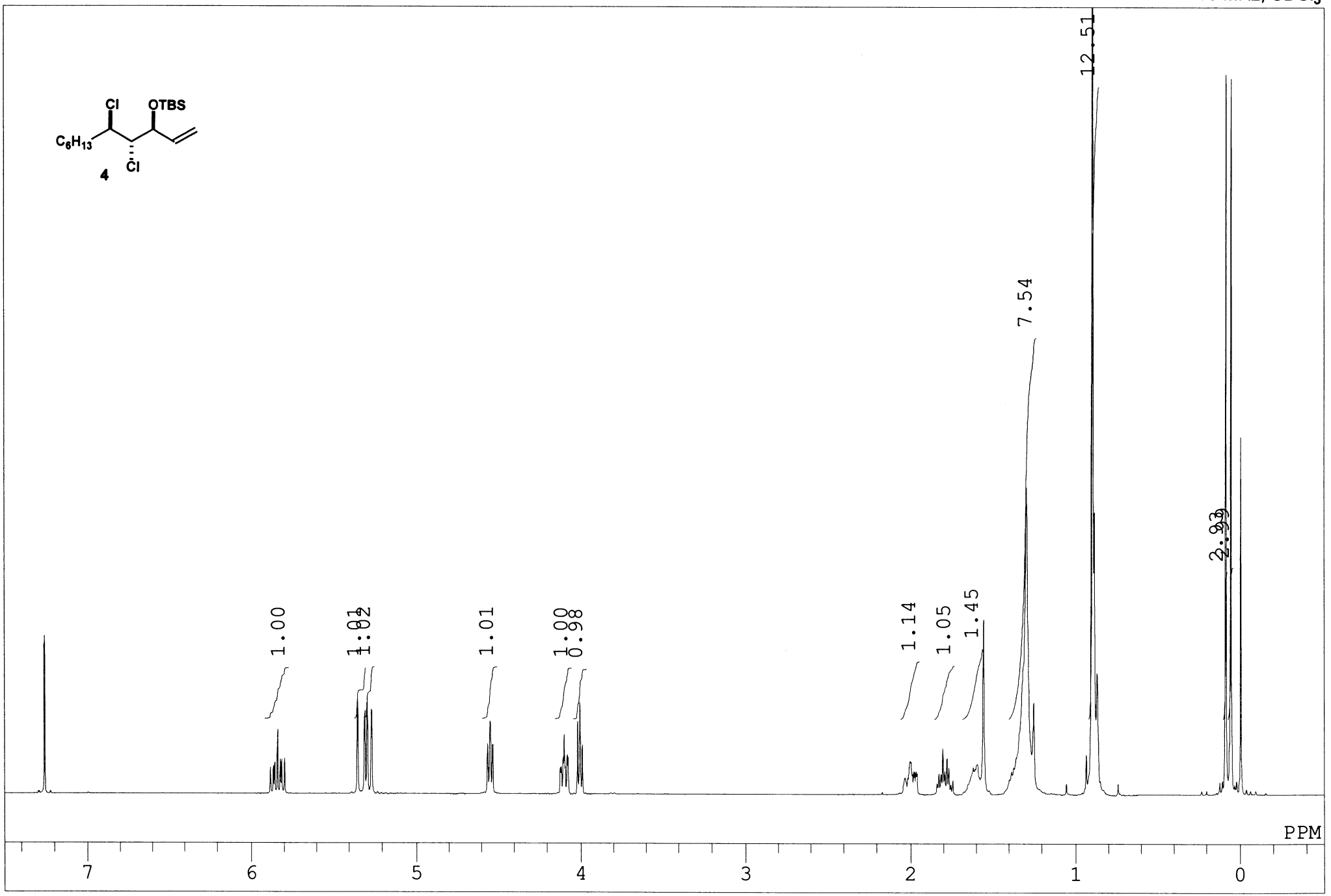

400 MHz, CDCl3
Cl
Cl
I
OTBS
16
2.05
2.00
1.94
1.95
2.54
10.05
9.52
5.94
PPM
7
6
5
4
3
2
1
0

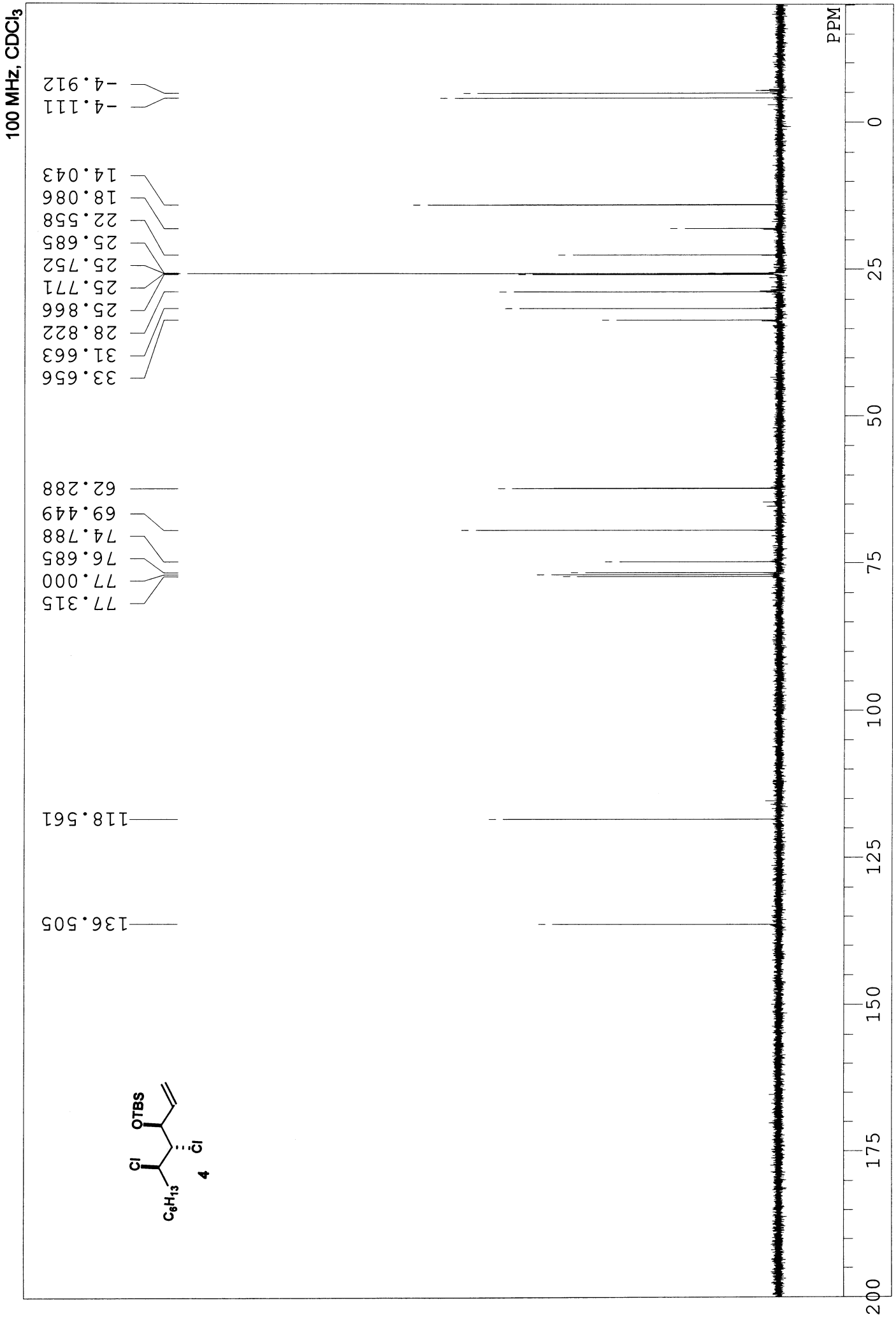
100 MHz, $CDCl_3$

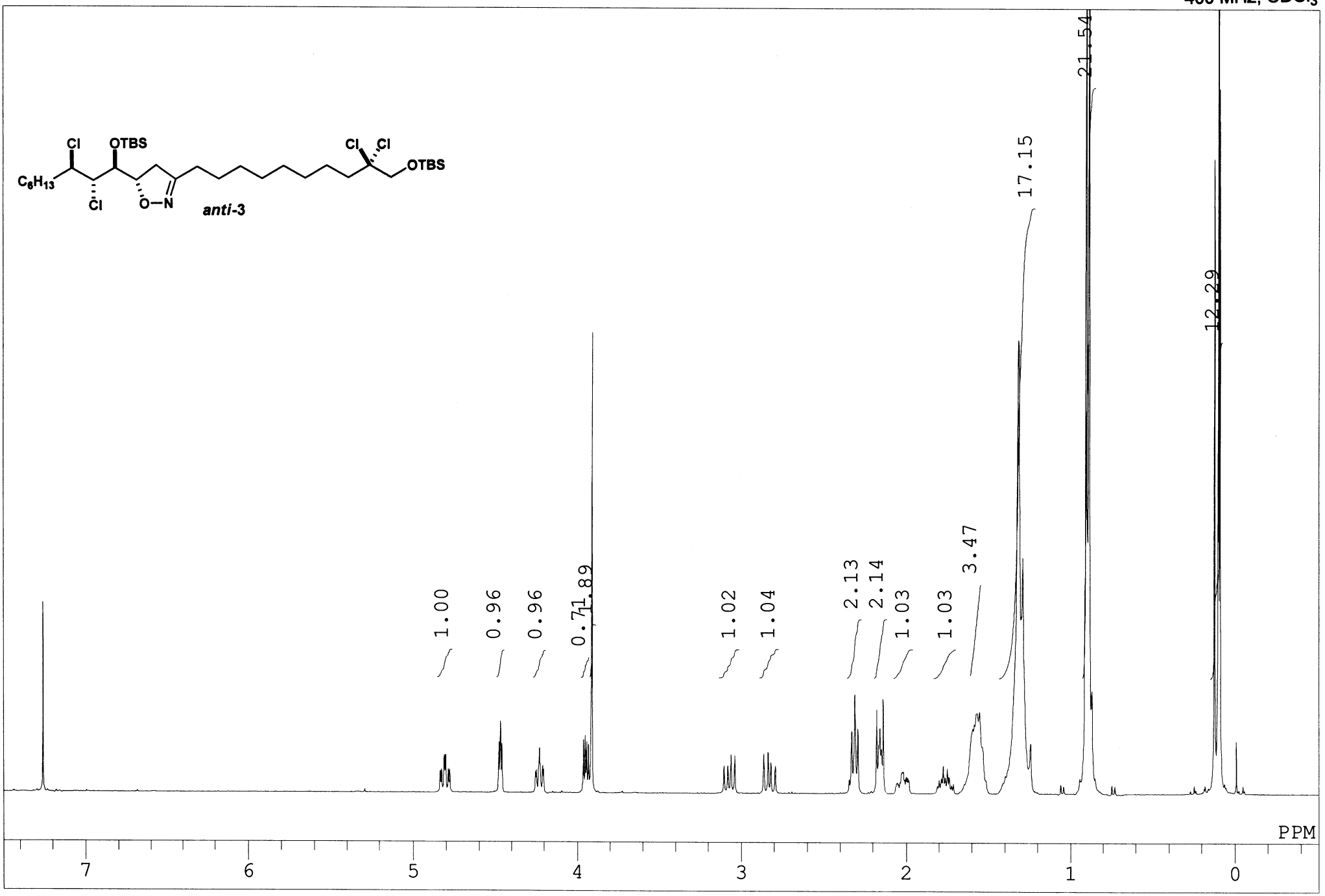


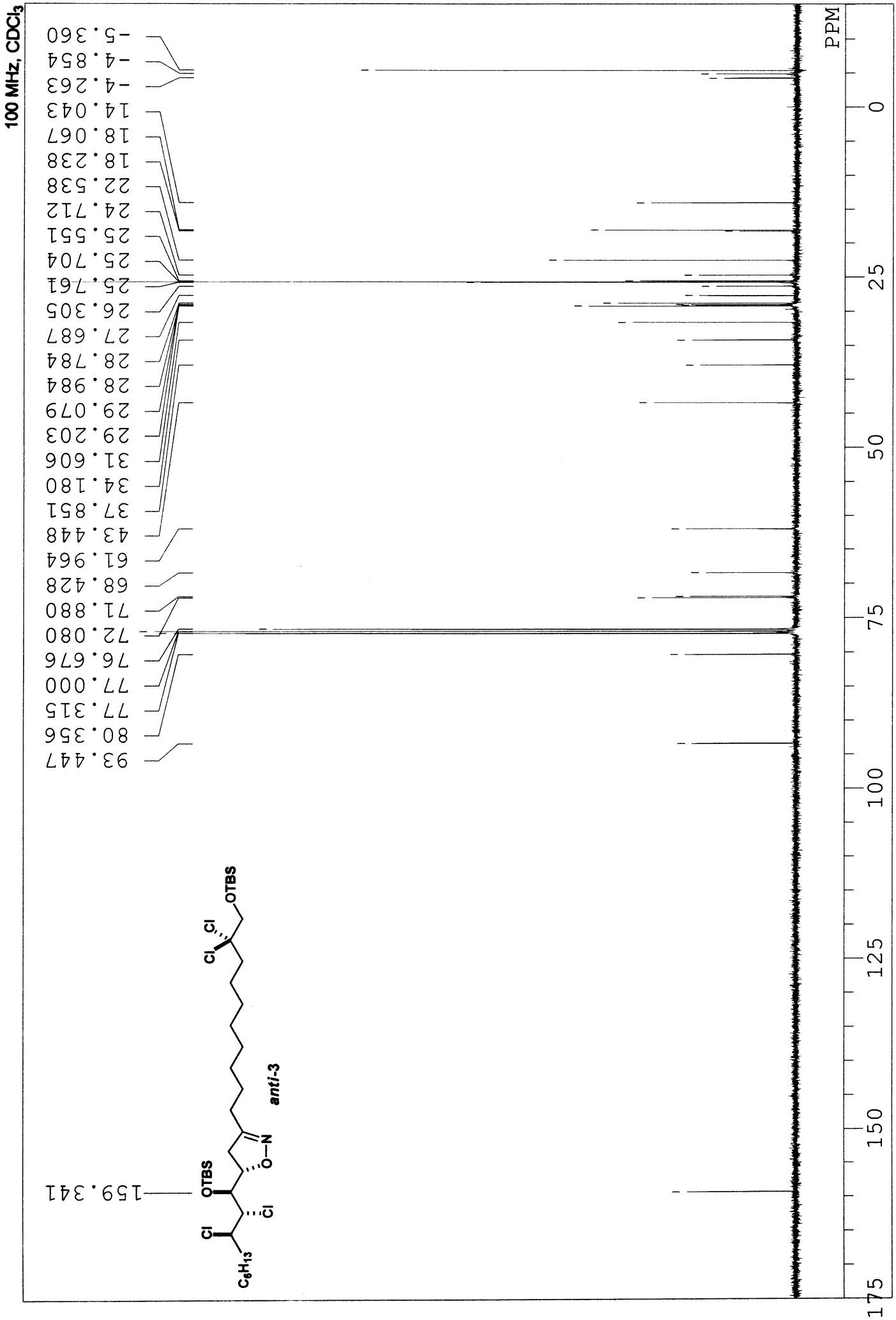

400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
5.95
9.62
10.12
2.11
2.10
2.13
2.14
2.00
OTBS
Cl
Cl
O2N
5


100 MHz, CDCl3
5.388
18.219
24.655
25.675
26.152
27.334
28.745
28.908
29.041
29.136
43.410
72.080
75.665
76.676
77.000
77.315
93.419
OTBS
Cl
Cl
O2N
5
PPM
0
25
50
75
100
125

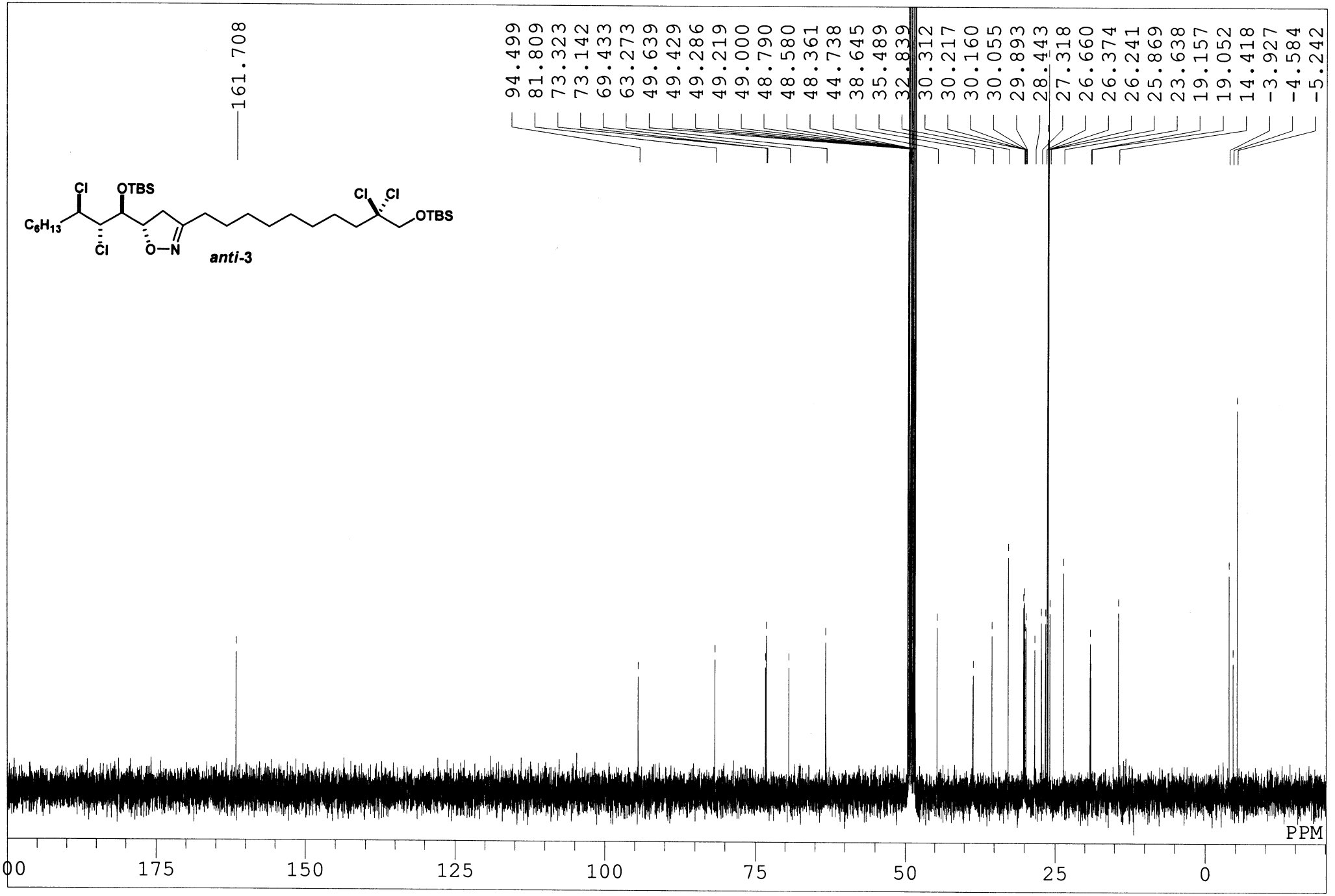

400 MHz, CDCl3
Cl
OTBS
C6H13
Cl
4
12.51
7.54
1.00
1.01
1.01
1.01
1.00
0.98
1.14
1.05
1.45
2.93
2.93
PPM
7
6
5
4
3
2
1
0

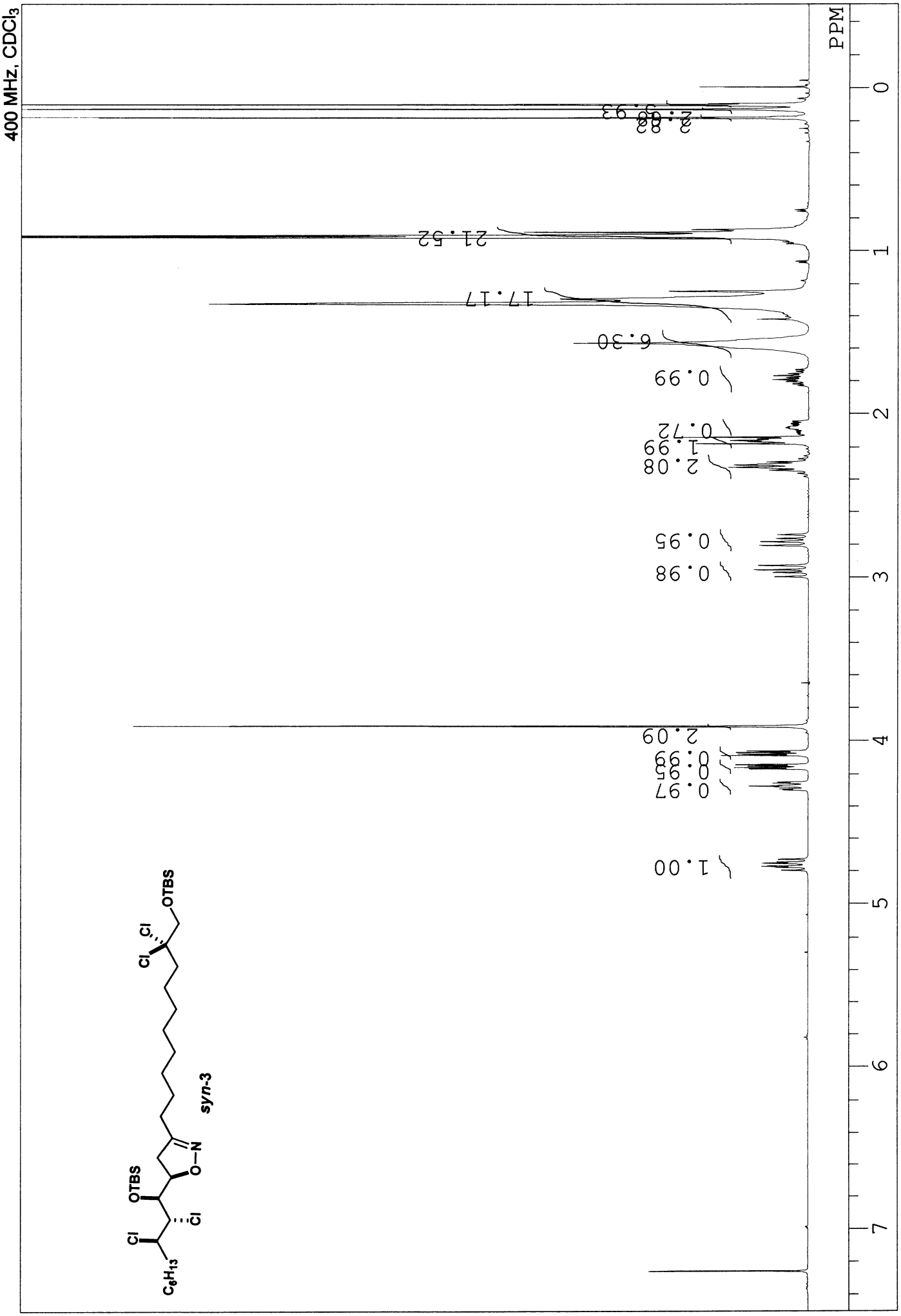

100 MHz, CDCl3
-4.912
-4.111
14.043
18.086
22.558
25.685
25.752
25.771
25.866
28.822
31.663
33.656
62.288
69.449
74.788
76.685
77.000
77.315
118.561
136.505
PPM
0
25
50
75
100
125
150
175
200
OTBS
Cl
Cl
C6H13
4

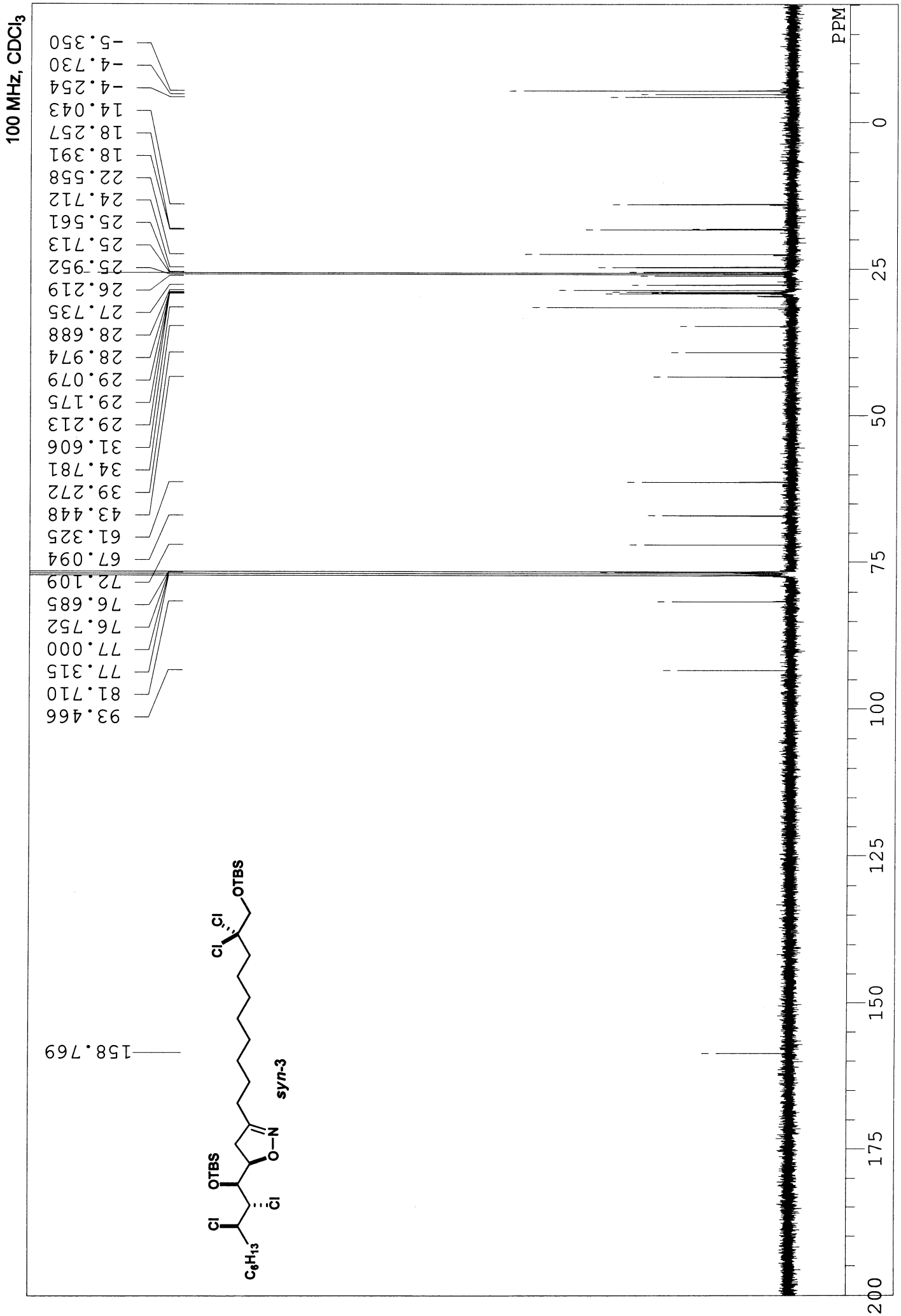

400 MHz, CDCl3
Cl
OTBS
Cl
Cl
OTBS
C6H13
Cl
O—N
anti-3
1.00
0.96
0.96
0.71
1.89
1.02
1.04
2.13
2.14
1.03
1.03
3.47
17.15
21.54
12.29
PPM
7
6
5
4
3
2
1
0


100 MHz, CDCl3
-5.360
-4.854
-4.263
14.043
18.067
18.238
22.538
24.712
25.551
25.704
25.761
26.305
27.687
28.784
28.984
29.079
29.203
31.606
34.180
37.851
43.448
61.964
68.428
71.880
72.080
76.676
77.000
77.315
80.356
93.447
159.341
OTBS
Cl
Cl
C6H13
Cl
OTBS
O—N
anti-3
PPM
0
25
50
75
100
125
150
175

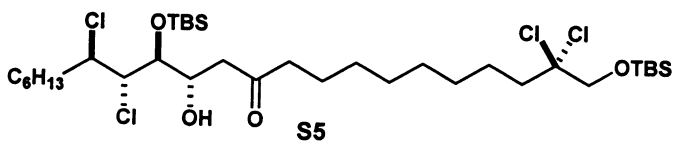
100 MHz, CD_3OD



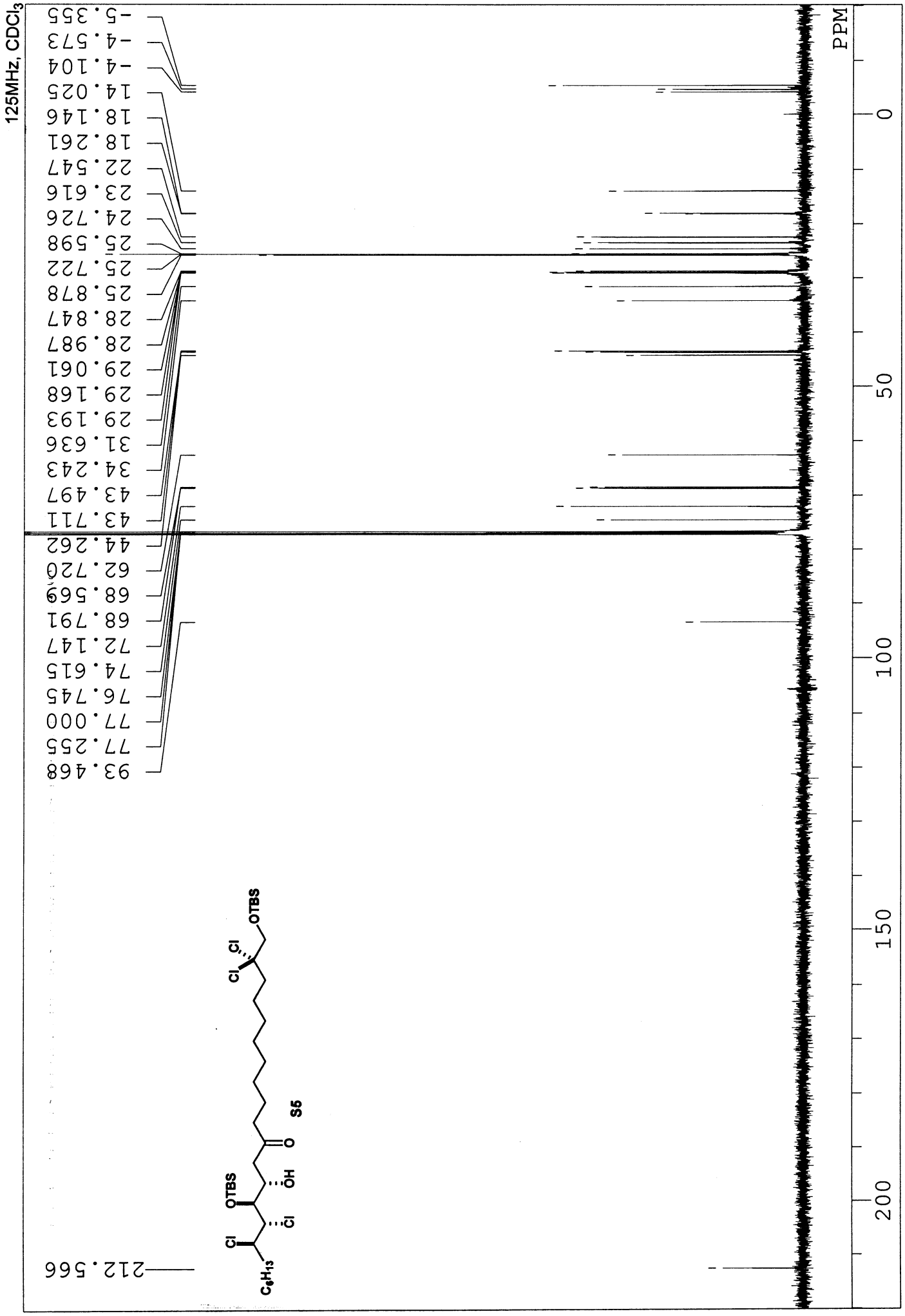

400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
23.93
22.88
21.52
17.17
6.30
0.99
0.72
1.99
2.08
0.95
0.98
2.09
0.99
0.95
0.97
1.00
OTBS
Cl
Cl
OTBS
Cl
Cl
O—N
C6H13
syn-3

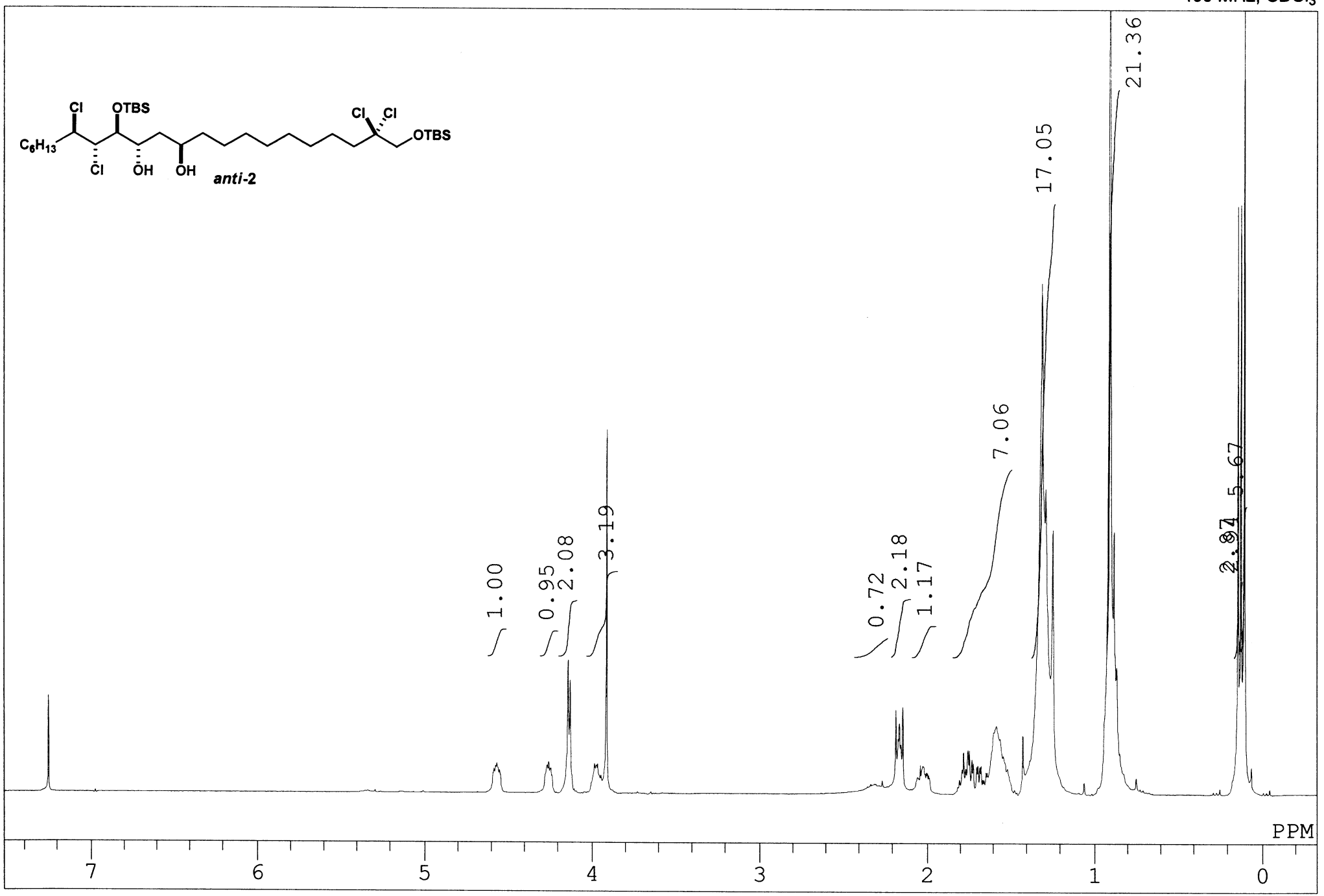

100 MHz, CDCl3
PPM
-5.350
-4.730
-4.254
14.043
18.257
18.391
22.558
24.712
25.561
25.713
25.952
26.219
27.735
28.688
28.974
29.079
29.175
29.213
31.606
34.781
39.272
43.448
61.325
67.094
72.109
76.685
76.752
77.000
77.315
81.710
93.466
158.769
OTBS
Cl
Cl
OTBS
Cl
Cl
O—N
syn-3
C6H13

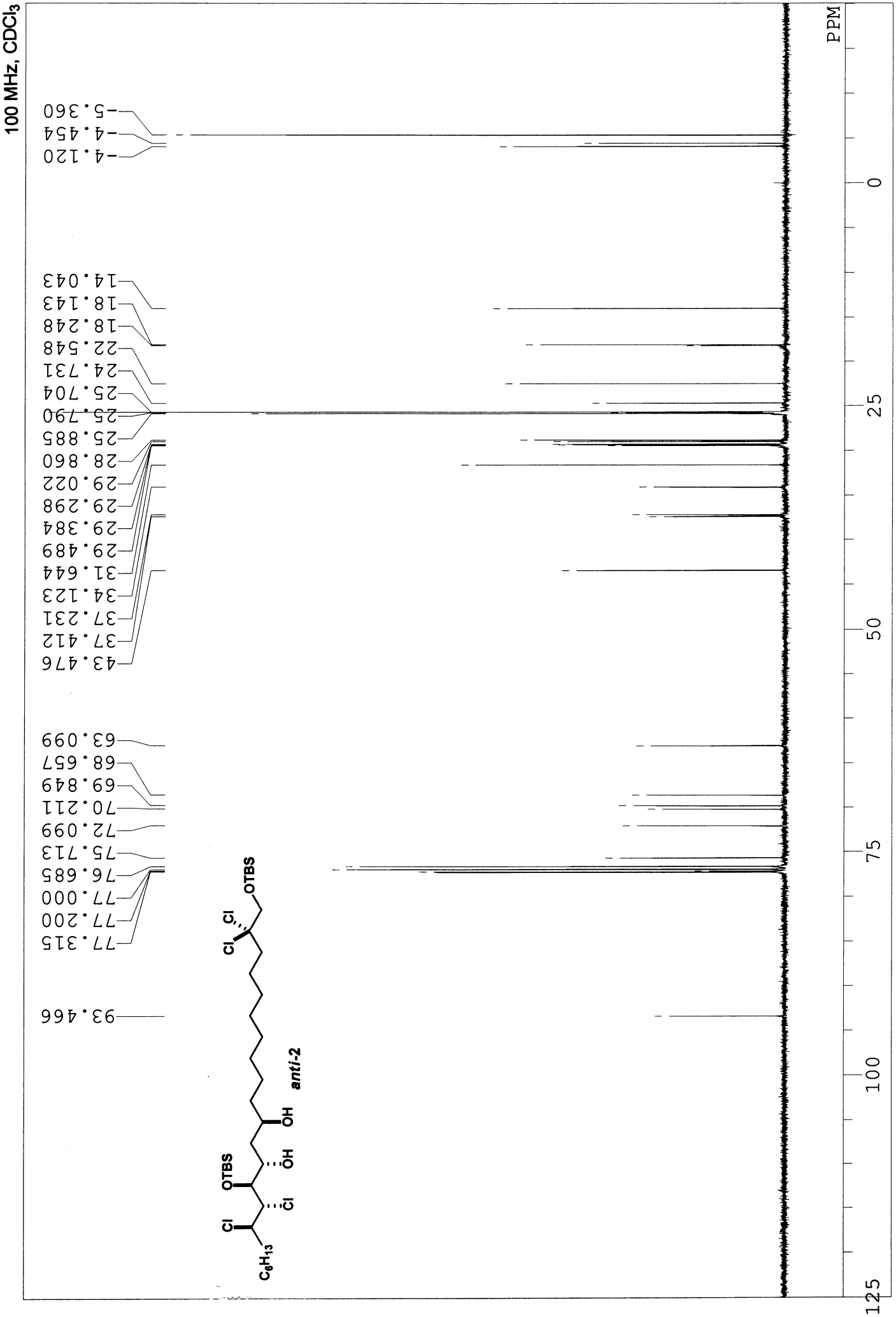
400 MHz, $CDCl_3$

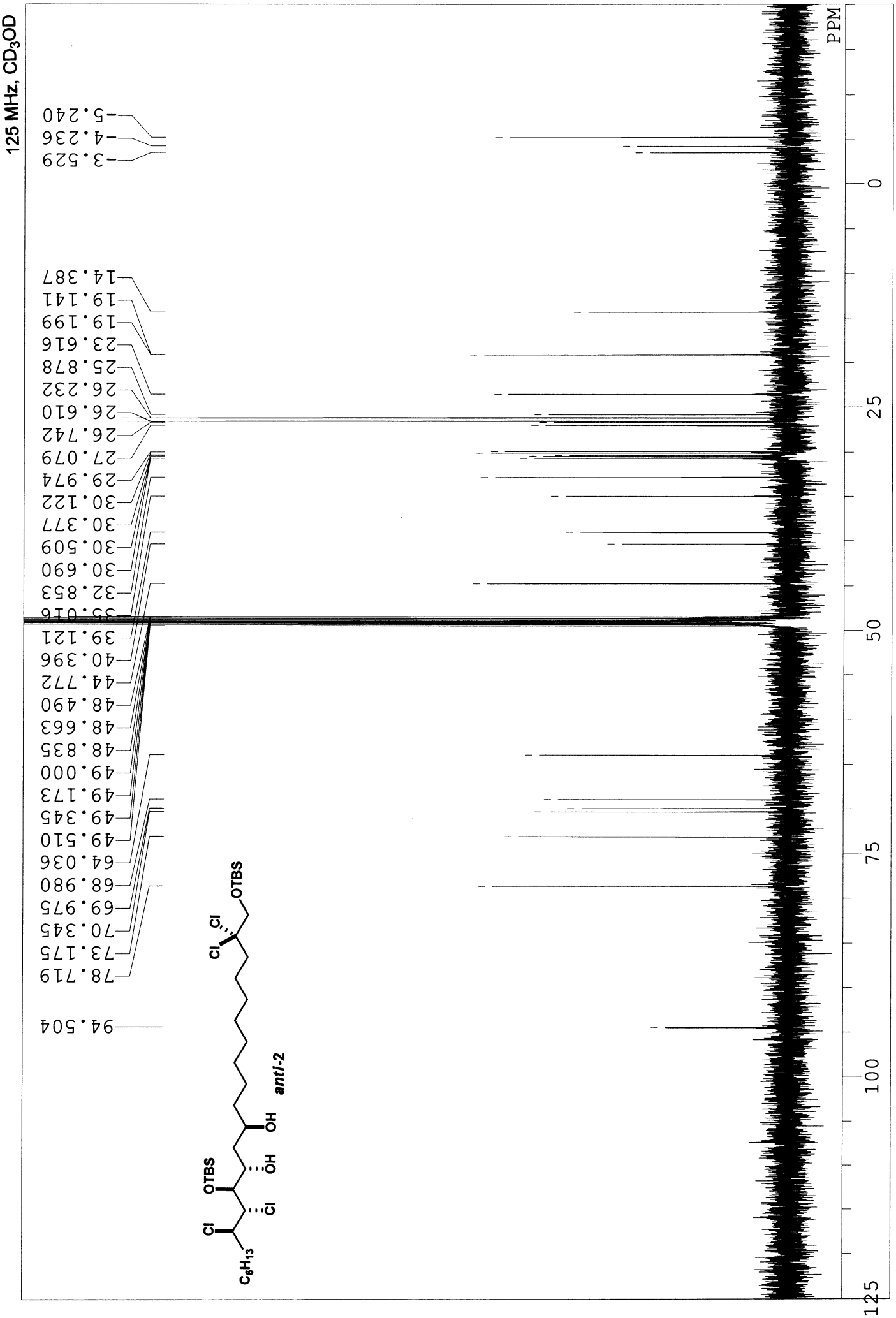


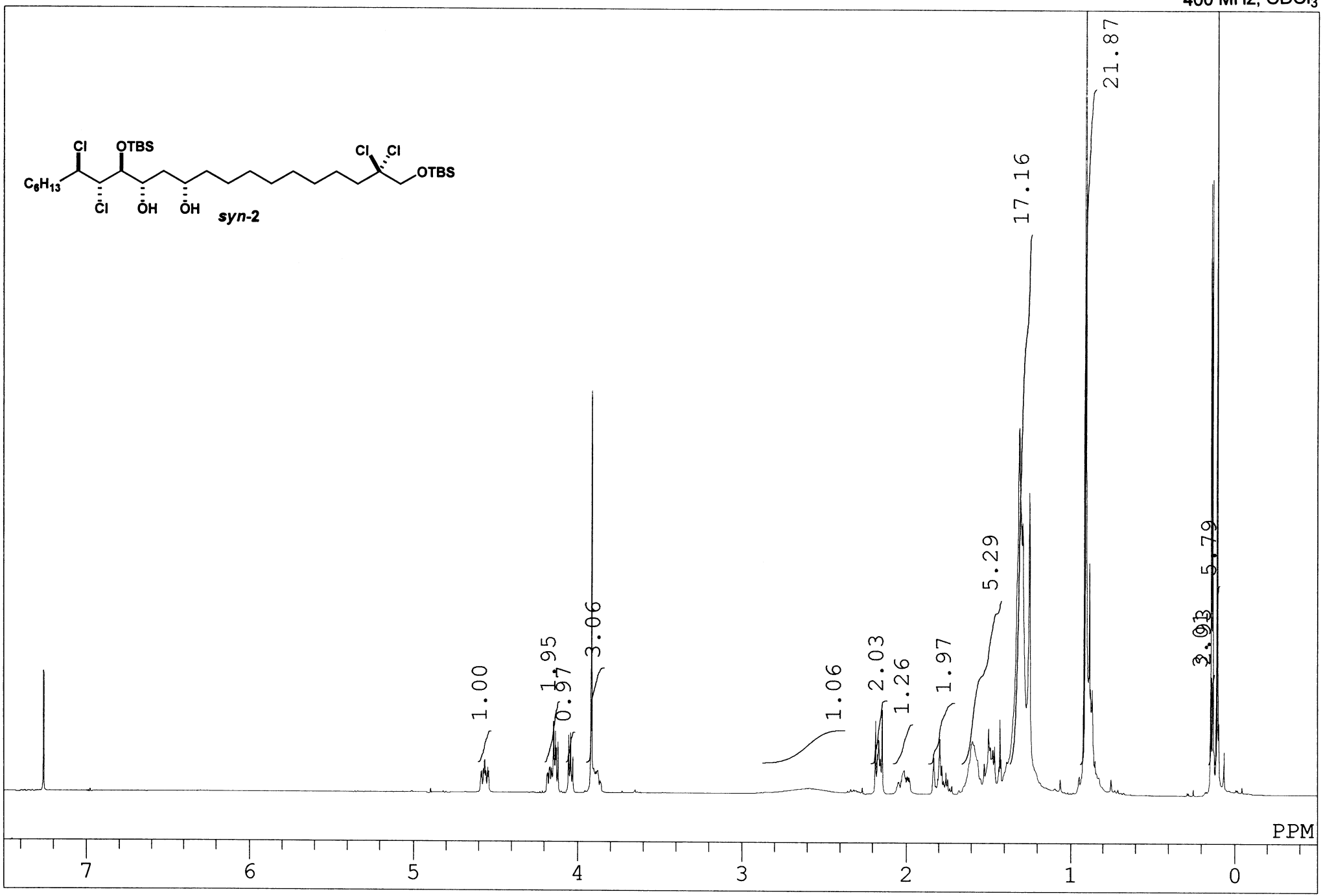
S5

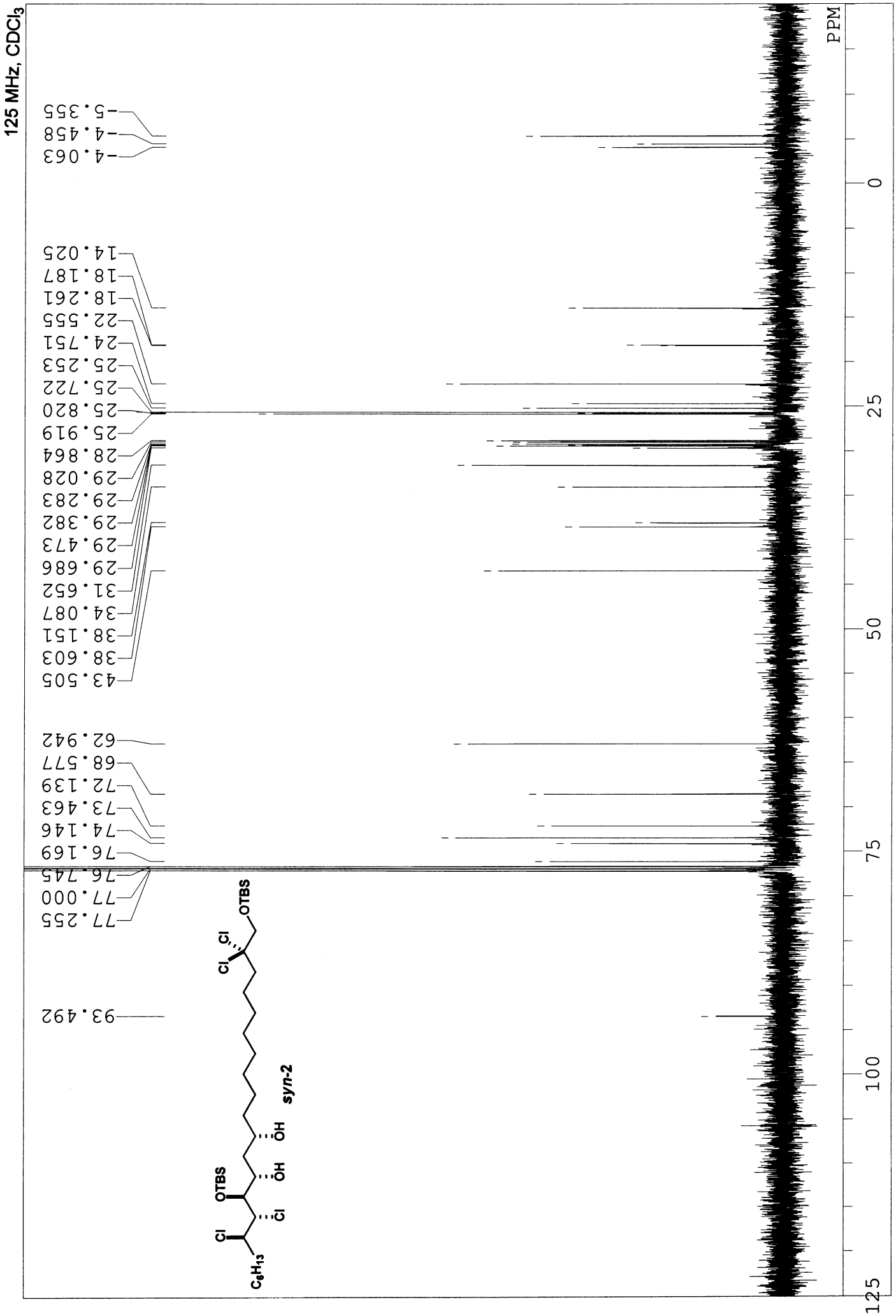

125MHz, CDCl3
-5.355
-4.573
-4.104
14.025
18.146
18.261
22.547
23.616
24.726
25.598
25.722
25.878
28.847
28.987
29.061
29.168
29.193
31.636
34.243
43.497
43.711
44.262
62.720
68.569
68.791
72.147
74.615
76.745
77.000
77.255
93.468
212.566
PPM
0
50
100
150
200
OTBS
Cl
Cl
OTBS
Cl
OH
Cl
O
S5
C6H13

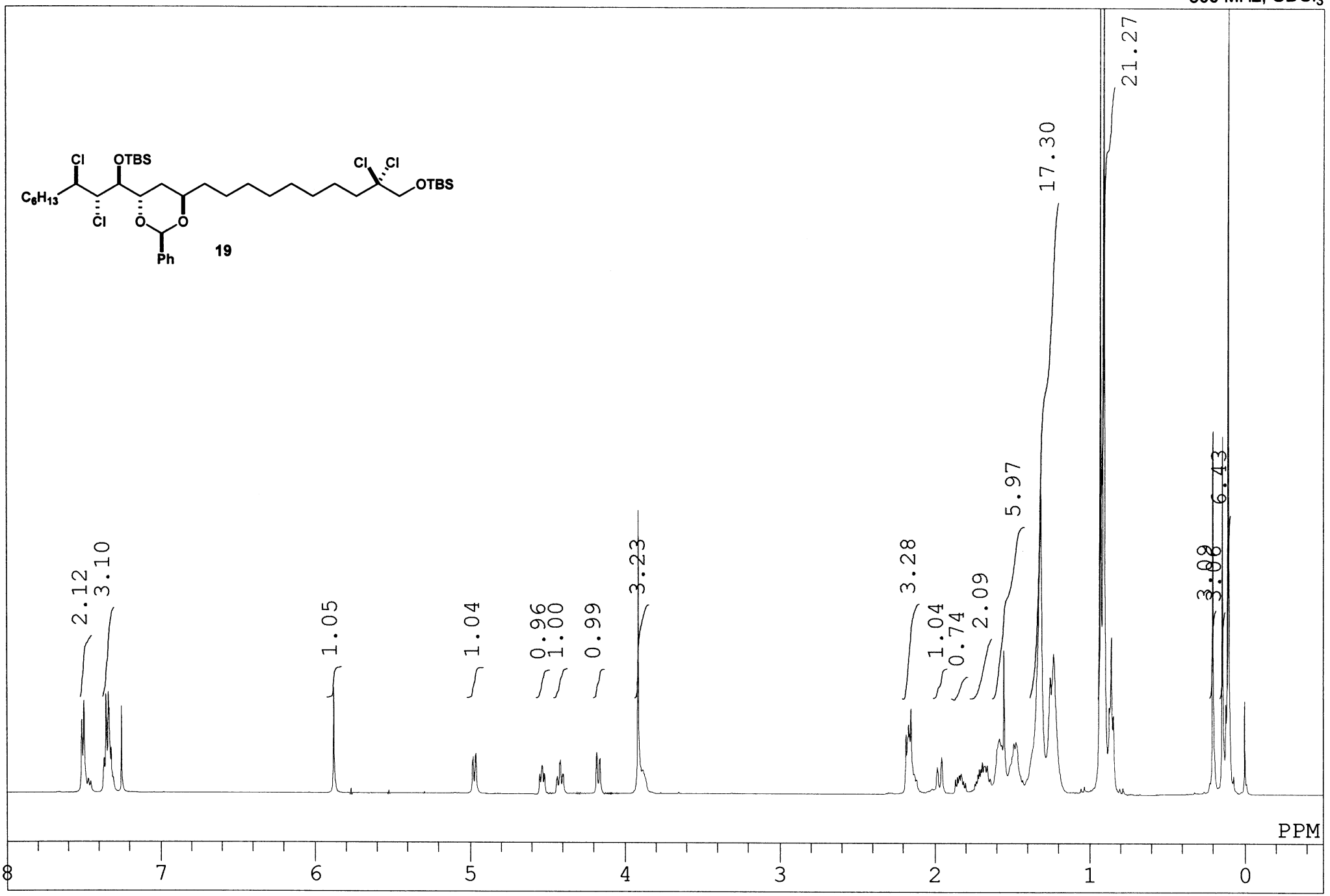

400 MHz, CDCl3
Cl
OTBS
Cl
Cl
C6H13
Cl
OH
OH
OTBS
anti-2
1.00
0.95
2.08
3.19
0.72
2.18
1.17
7.06
17.05
21.36
2.87
5.67
PPM
7
6
5
4
3
2
1
0


100 MHz, CDCl3
-5.360
-4.454
-4.120
14.043
18.143
18.248
22.548
24.731
25.704
25.790
25.885
28.860
29.022
29.298
29.384
29.489
31.644
34.123
37.231
37.412
43.476
63.099
68.657
69.849
70.211
72.099
75.713
76.685
77.000
77.200
77.315
93.466
PPM
0
25
50
75
100
125
OTBS
Cl
Cl
OH
OH
Cl
OTBS
Cl
C6H13
anti-2

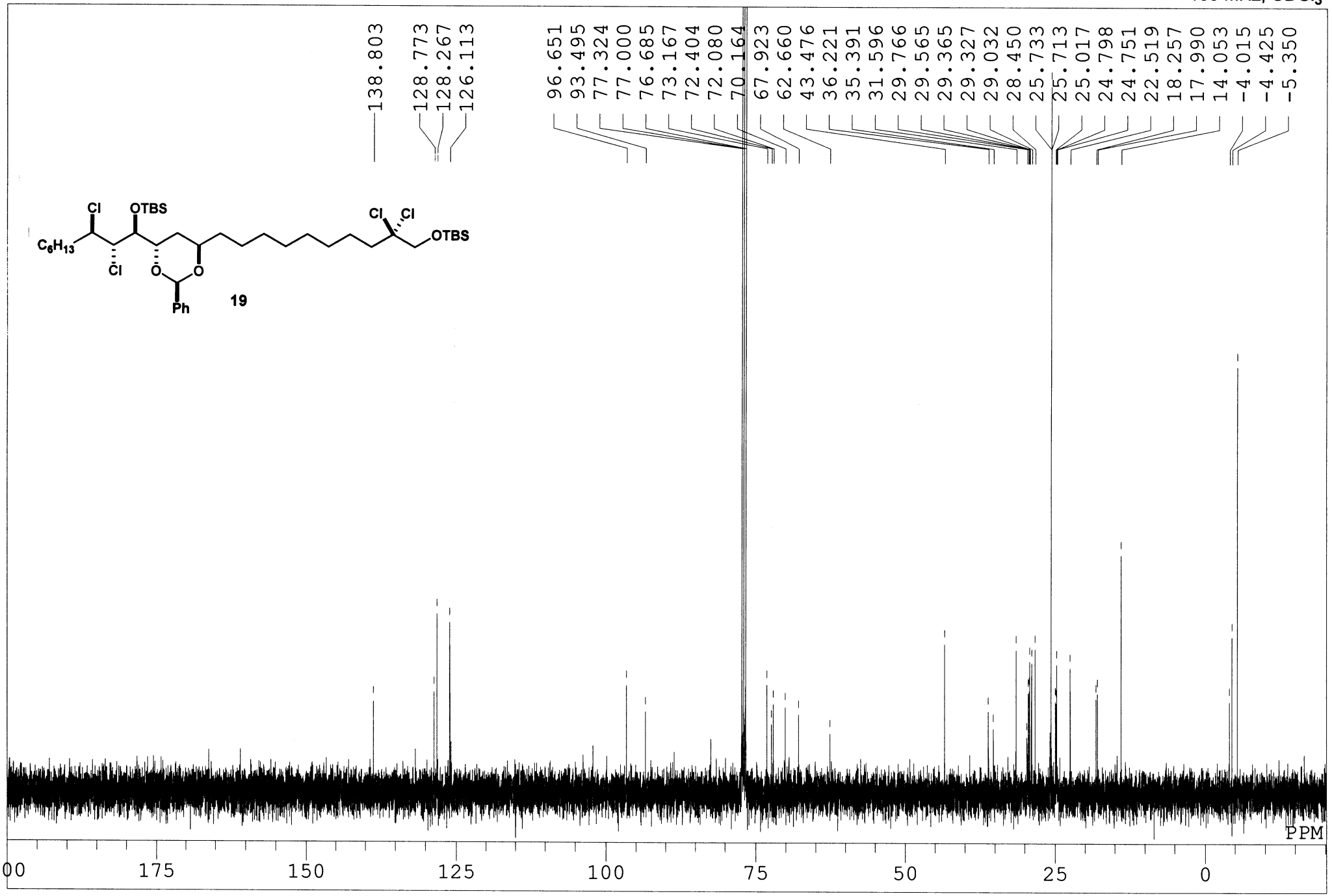

125 MHz, CD3OD
-5.240
-4.236
-3.529
14.387
19.141
19.199
23.616
25.878
26.232
26.610
26.742
27.079
29.974
30.122
30.377
30.509
30.690
32.853
35.016
39.121
40.396
44.772
48.490
48.663
48.835
49.000
49.173
49.345
49.510
64.036
68.980
69.975
70.345
73.175
78.719
94.504
PPM
0
25
50
75
100
125
OTBS
Cl
Cl
Cl
OH
OH
OTBS
Cl
C8H13
anti-2


400 MHz, CDCl3
Cl
OTBS
Cl
Cl
C6H13
Cl
OH
OH
OTBS
syn-2
1.00
1.95
0.97
3.06
1.06
2.03
1.26
1.97
5.29
17.16
21.87
3.01
3.03
5.79
PPM
7
6
5
4
3
2
1
0

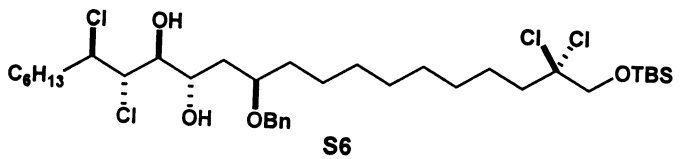

125 MHz, CDCl3
-5.355
-4.458
-4.063
14.025
18.187
18.261
22.555
24.751
25.253
25.722
25.820
25.919
28.864
29.028
29.283
29.382
29.473
29.686
31.652
34.087
38.151
38.603
43.505
62.942
68.577
72.139
73.463
74.146
76.169
76.745
77.000
77.255
93.492
PPM
0
25
50
75
100
125
OTBS
Cl
Cl
OH
OH
Cl
OTBS
Cl
C6H13
syn-2


500 MHz, CDCl3
Cl
OTBS
Cl
Cl
C6H13
Cl
O
O
OTBS
Ph
19
2.12
3.10
1.05
1.04
0.96
1.00
0.99
3.23
3.28
1.04
0.74
2.09
5.97
17.30
21.27
3.00
3.08
6.43
PPM
8
7
6
5
4
3
2
1
0

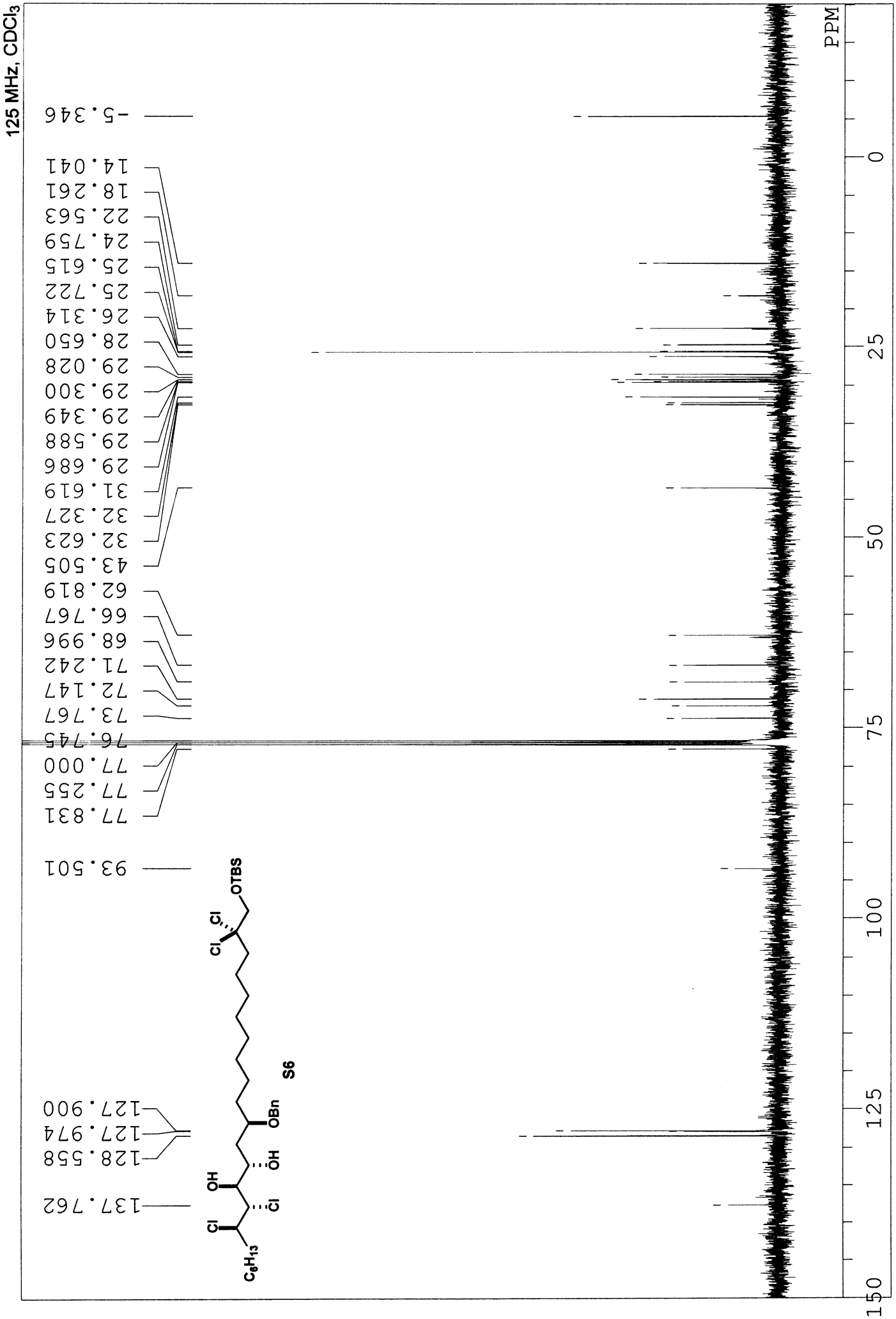
100 MHz, $CDCl_3$

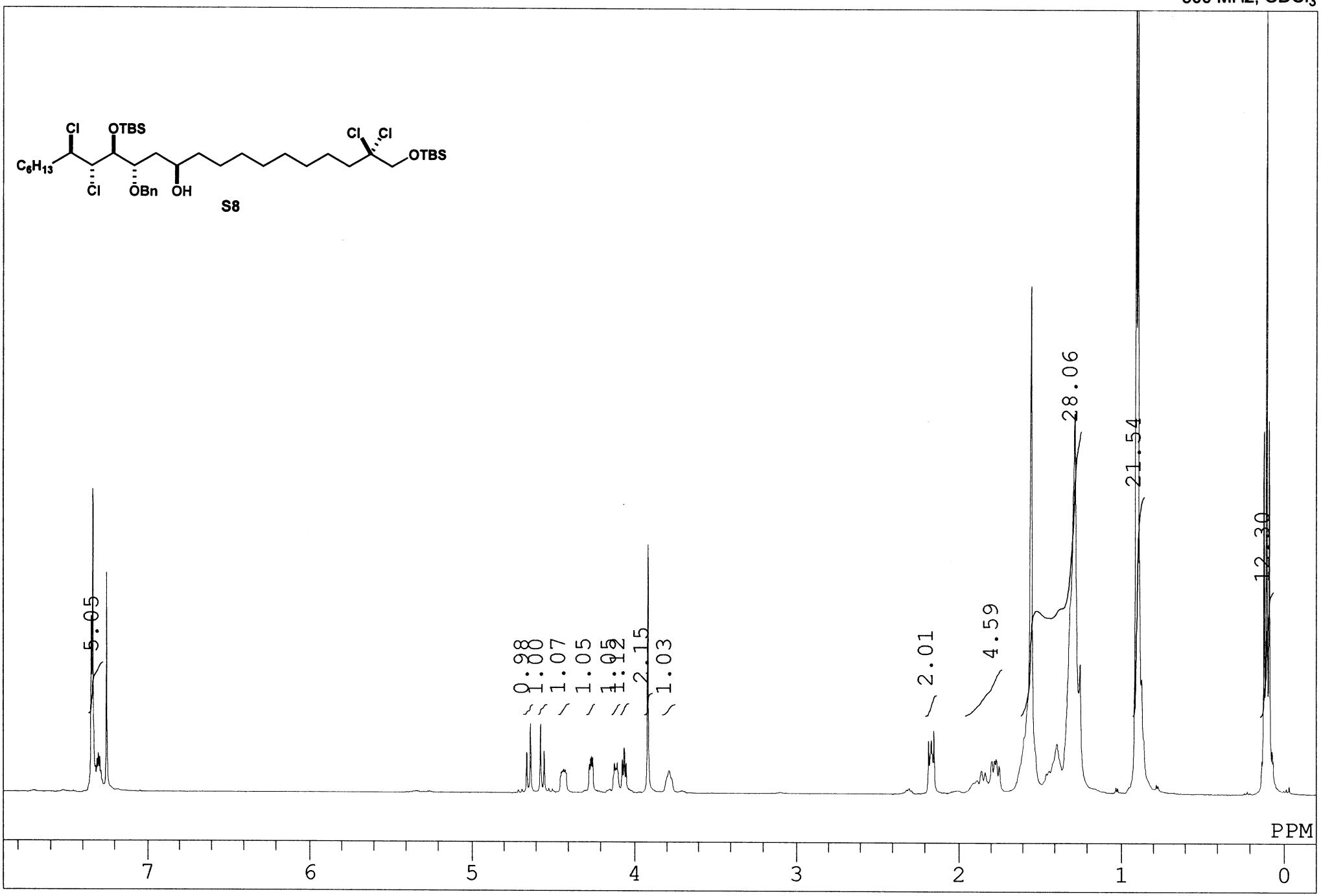


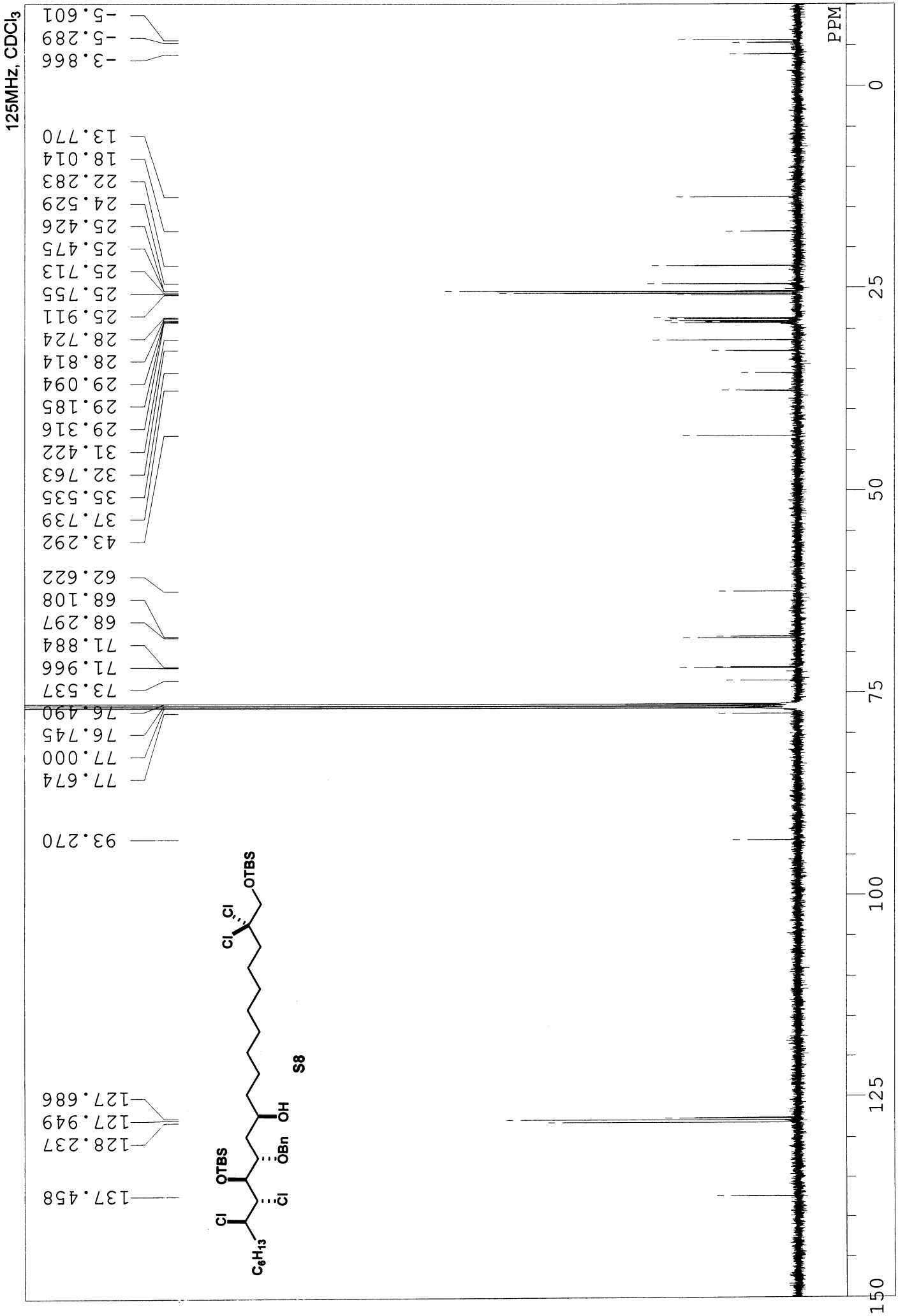
400 MHz, $CDCl_3$



S6

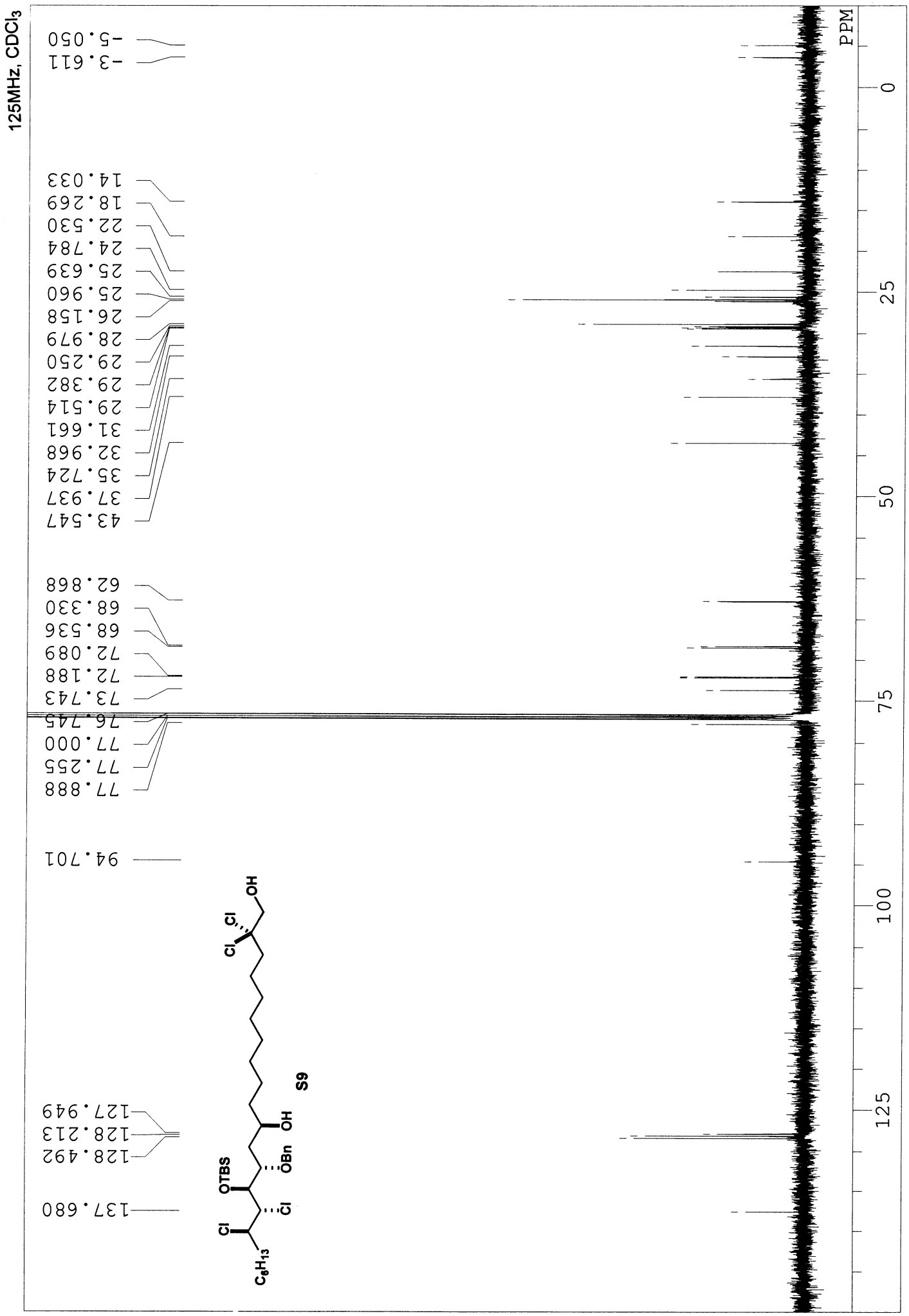

125 MHz, CDCl3
-5.346
14.041
18.261
22.563
24.759
25.615
25.722
26.314
28.650
29.028
29.300
29.349
29.588
29.686
31.619
32.327
32.623
43.505
62.819
66.767
68.996
71.242
72.147
73.767
76.745
77.000
77.255
77.831
93.501
127.900
127.974
128.558
137.762
PPM
0
25
50
75
100
125
150
OTBS
Cl
Cl
OBn
OH
OH
Cl
Cl
C6H13
S6

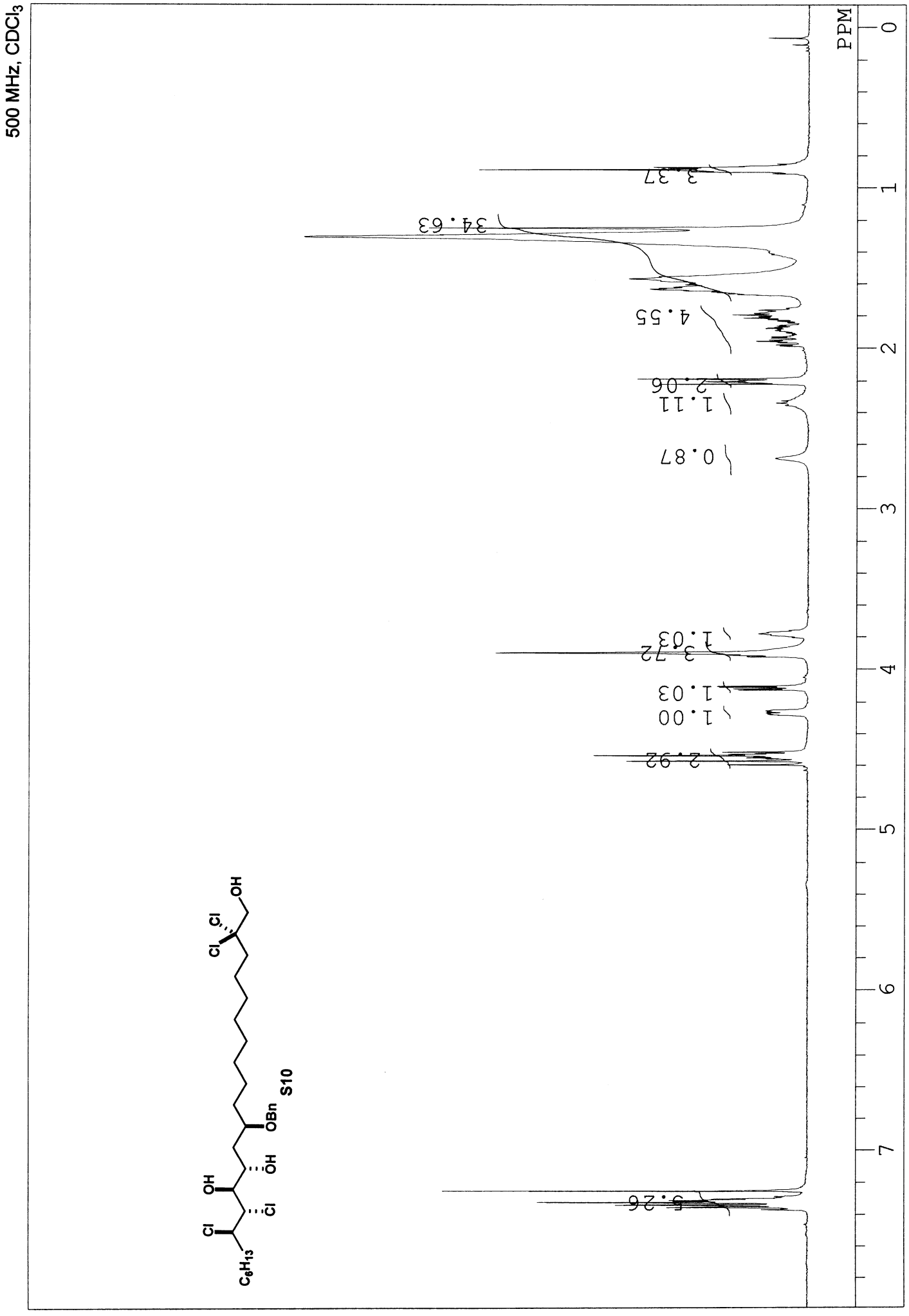

500 MHz, CDCl3
Cl
OTBS
C6H13
Cl
OBn
OH
Cl
Cl
OTBS
S8
5.05
0.88
1.00
1.07
1.05
1.05
1.12
2.15
1.03
2.01
4.59
28.06
21.54
12.30
PPM
7
6
5
4
3
2
1
0

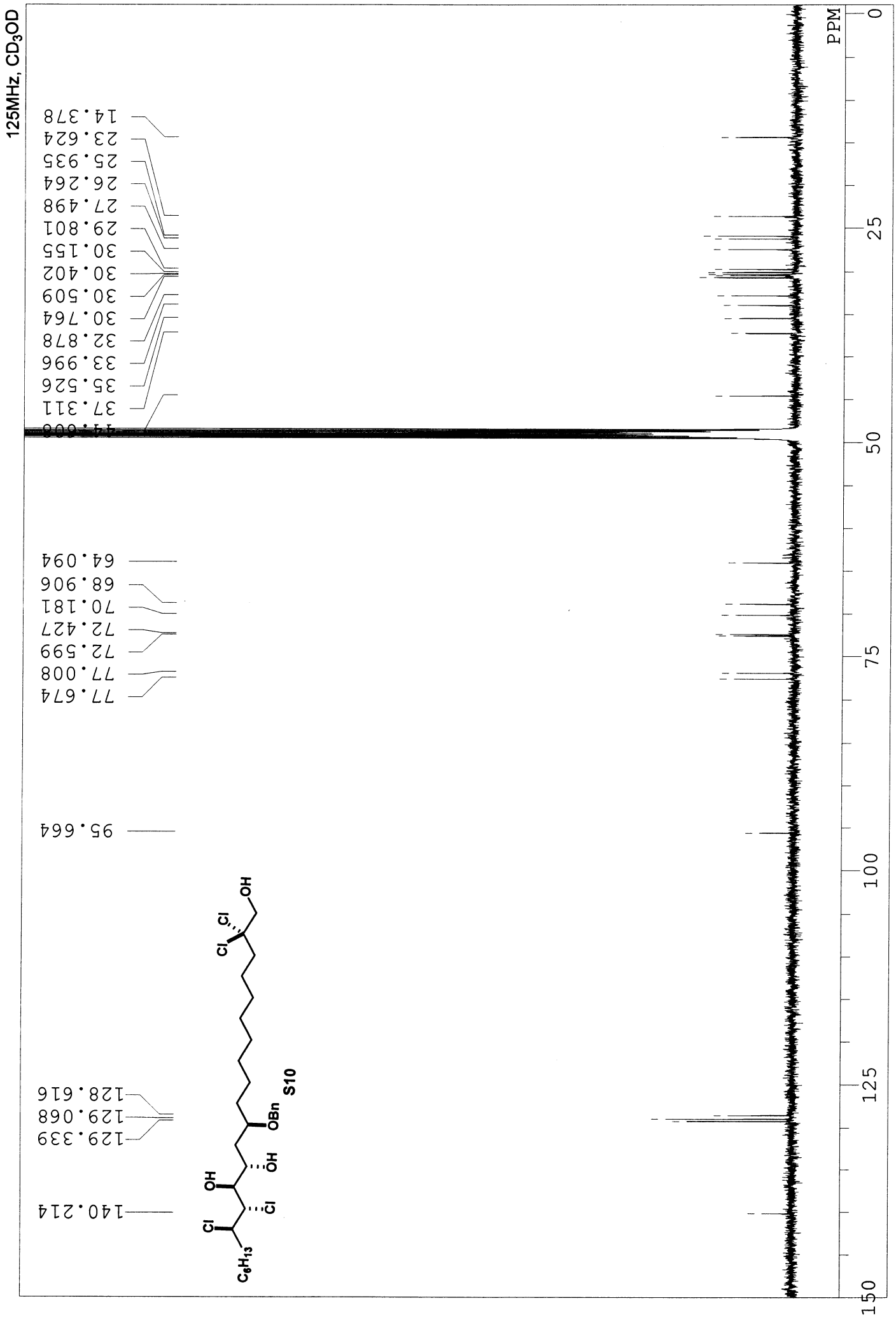

125MHz, CDCl3
-5.601
-5.289
-3.866
13.770
18.014
22.283
24.529
25.426
25.475
25.713
25.755
25.911
28.724
28.814
29.094
29.185
29.316
31.422
32.763
35.535
37.739
43.292
62.622
68.108
68.297
71.884
71.966
73.537
76.490
76.745
77.000
77.674
93.270
127.686
127.949
128.237
137.458
PPM
0
25
50
75
100
125
150
OTBS
Cl
Cl
OBn
OH
S8
OTBS
Cl
Cl
C8H13

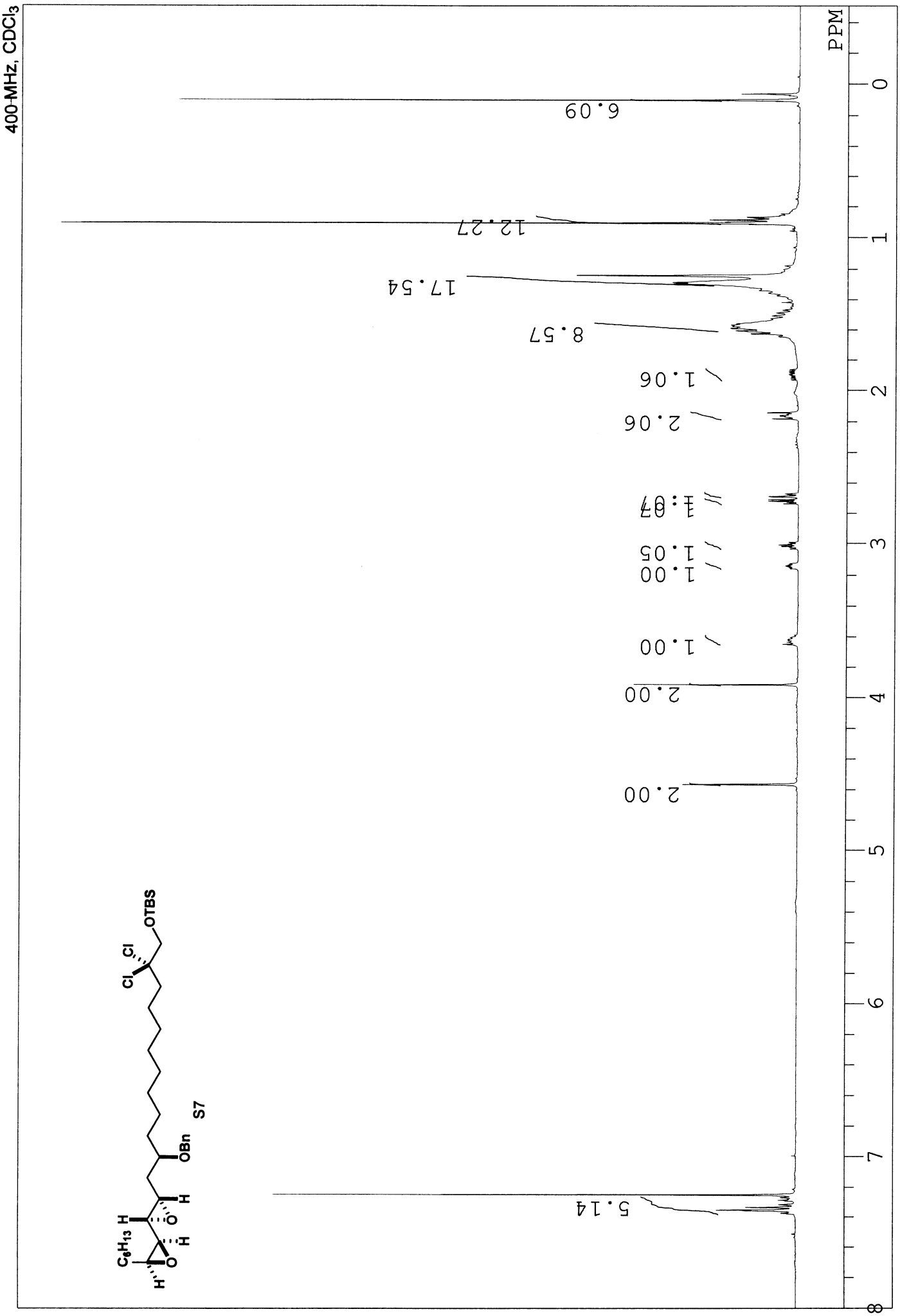
500 MHz, $CDCl_3$

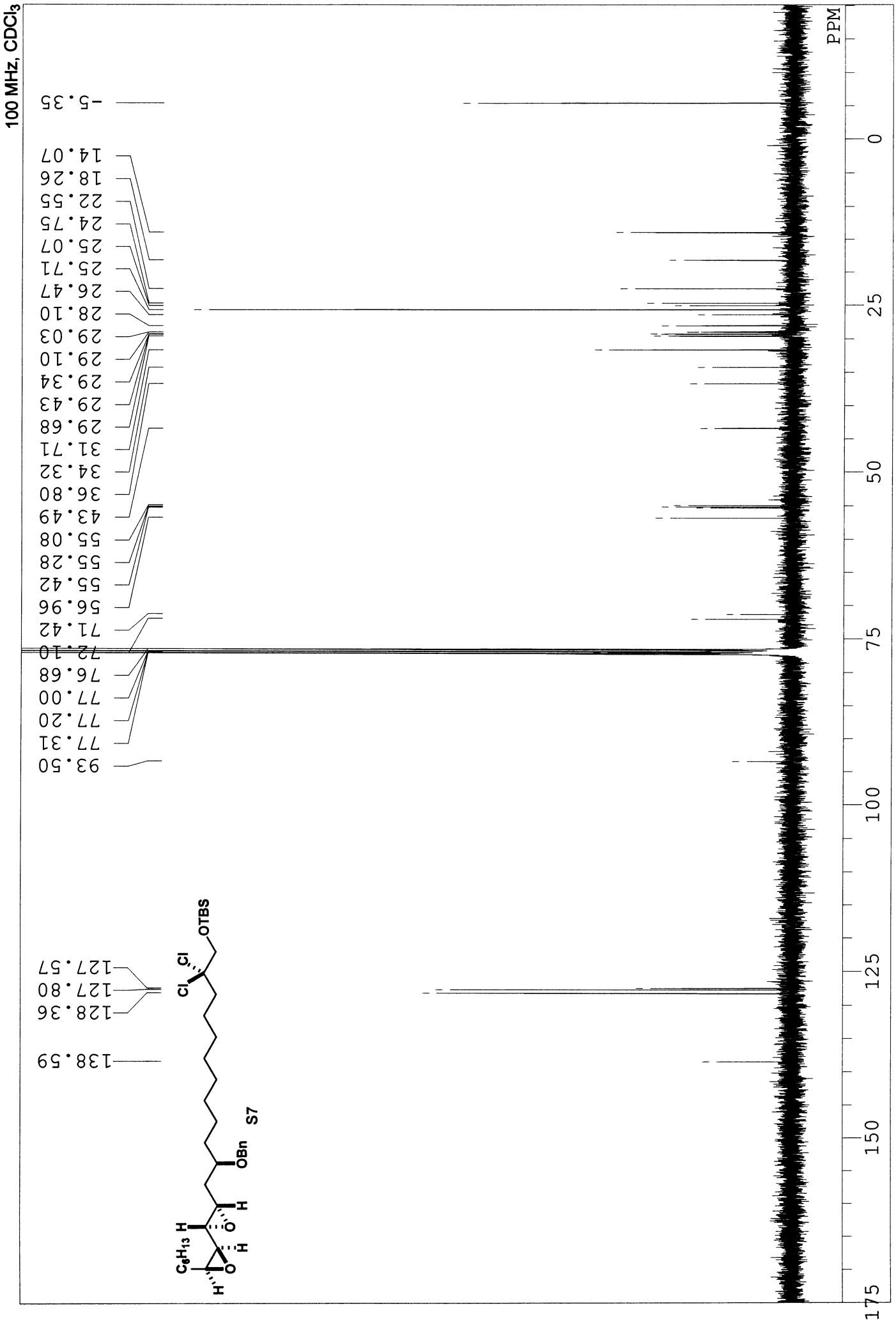
S9


125MHz, CDCl3
-5.050
-3.611
14.033
18.269
22.530
24.784
25.639
25.960
26.158
28.979
29.250
29.382
29.514
31.661
32.968
35.724
37.937
43.547
62.868
68.330
68.536
72.089
72.188
73.743
76.745
77.000
77.255
77.888
94.701
127.949
128.213
128.492
137.680
PPM
0
25
50
75
100
125
S9
OH
Cl
Cl
OBn
OTBS
Cl
Cl
C6H13

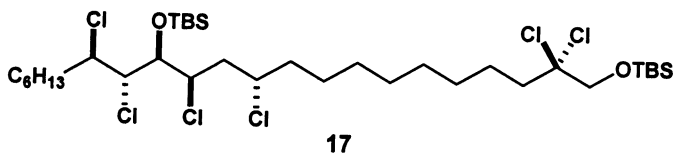

500 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
5.26
2.92
1.00
1.03
3.72
1.03
0.87
1.11
2.06
4.55
34.63
3.37
S10


125MHz, CD3OD
14.378
23.624
25.935
26.264
27.498
29.801
30.155
30.402
30.509
30.764
32.878
33.996
35.526
37.311
44.606
64.094
68.906
70.181
72.427
72.599
77.008
77.674
95.664
128.616
129.068
129.339
140.214
S10
PPM
0
25
50
75
100
125
150

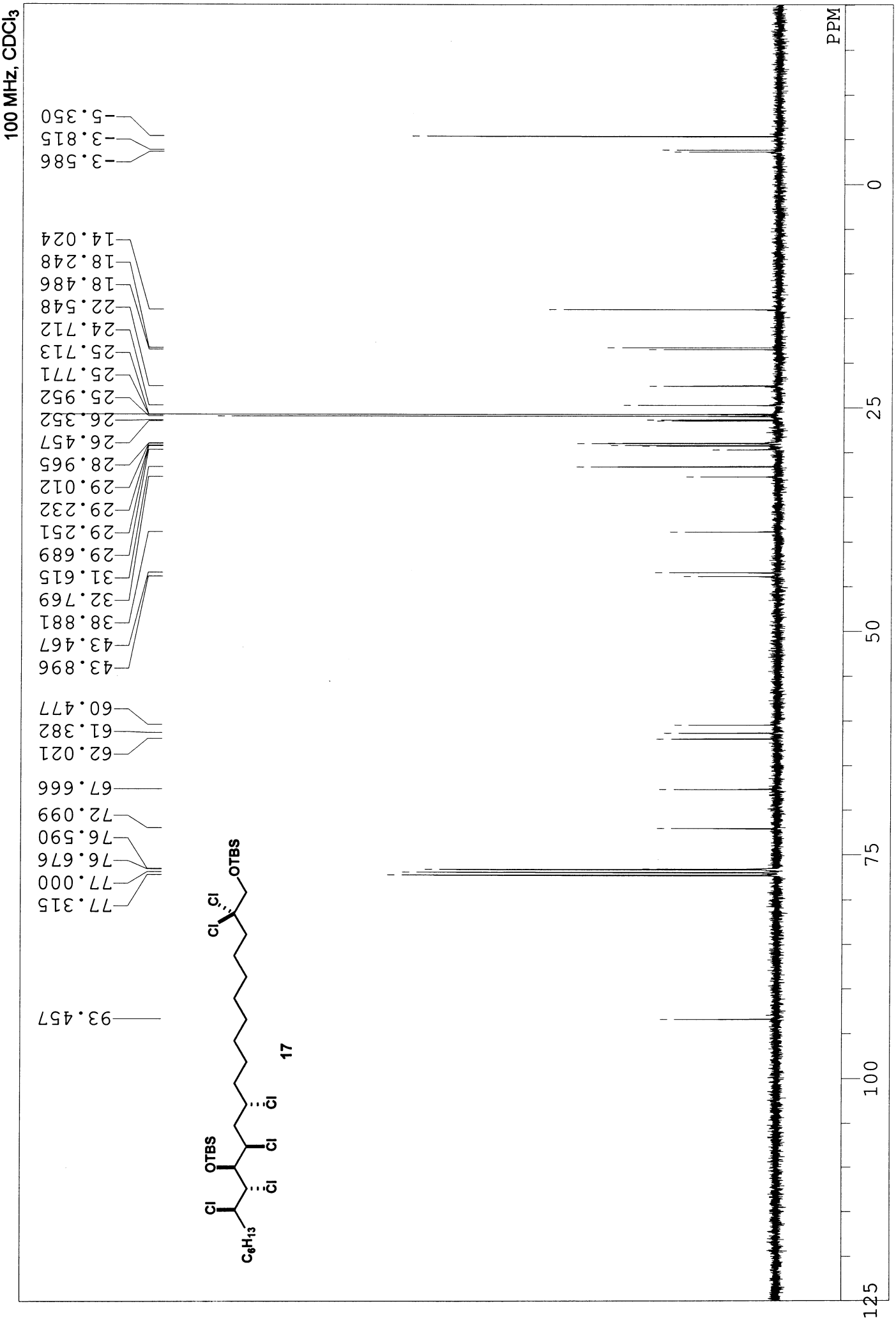

400-MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
8
5.14
2.00
2.00
1.00
1.00
1.05
1.07
2.06
1.06
8.57
17.54
12.27
6.09
OTBS
Cl
Cl
OBn
S7
C6H13
H
H
H
O
O
H

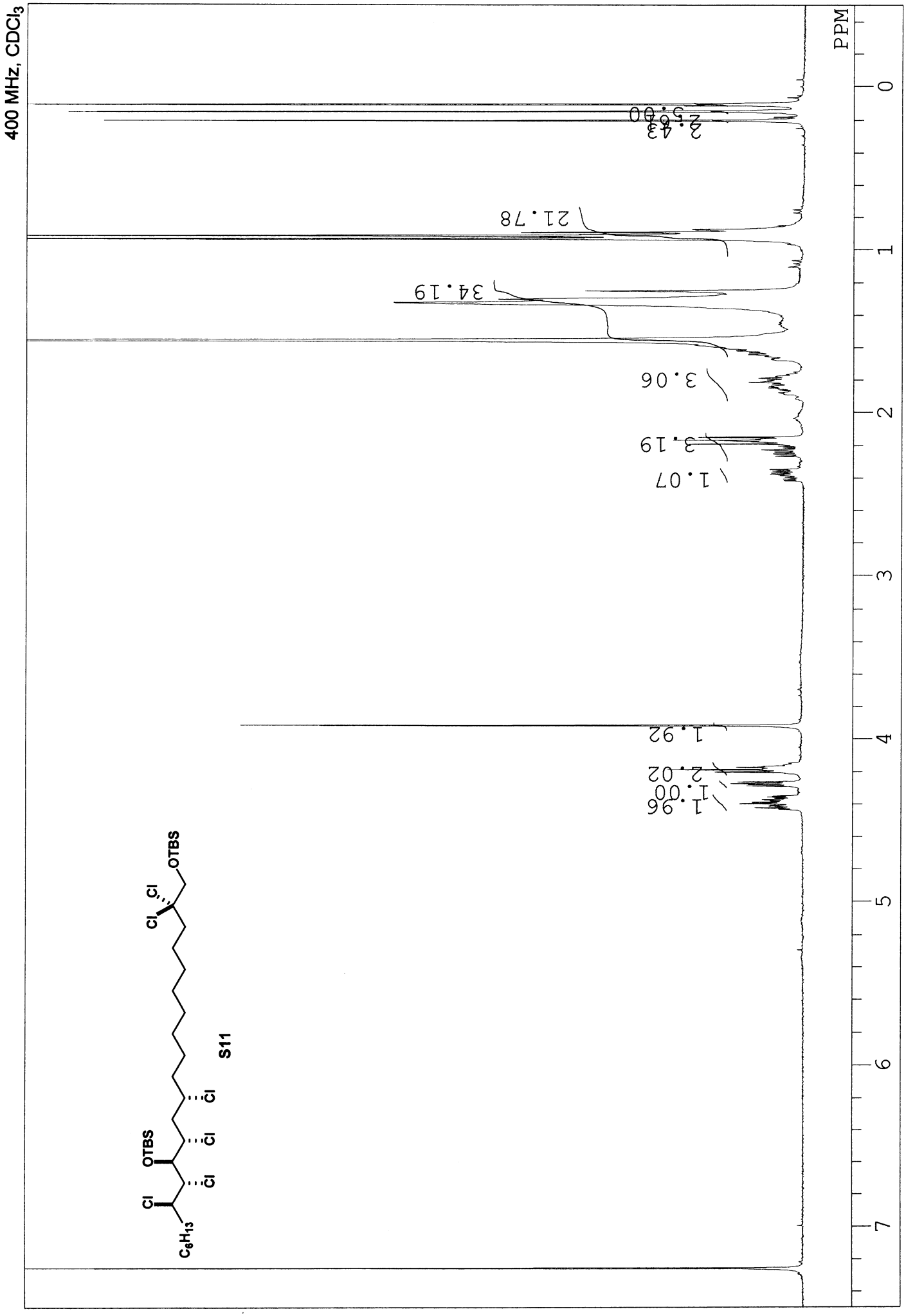

100 MHz, CDCl3
-5.35
14.07
18.26
22.55
24.75
25.07
25.71
26.47
28.10
29.03
29.10
29.34
29.43
29.68
31.71
34.32
36.80
43.49
55.08
55.28
55.42
56.96
71.42
72.10
76.68
77.00
77.20
77.31
93.50
127.57
127.80
128.36
138.59
PPM
0
25
50
75
100
125
150
175
OTBS
Cl
Cl
OBn
S7
H
O
H
H
O
H
C6H13

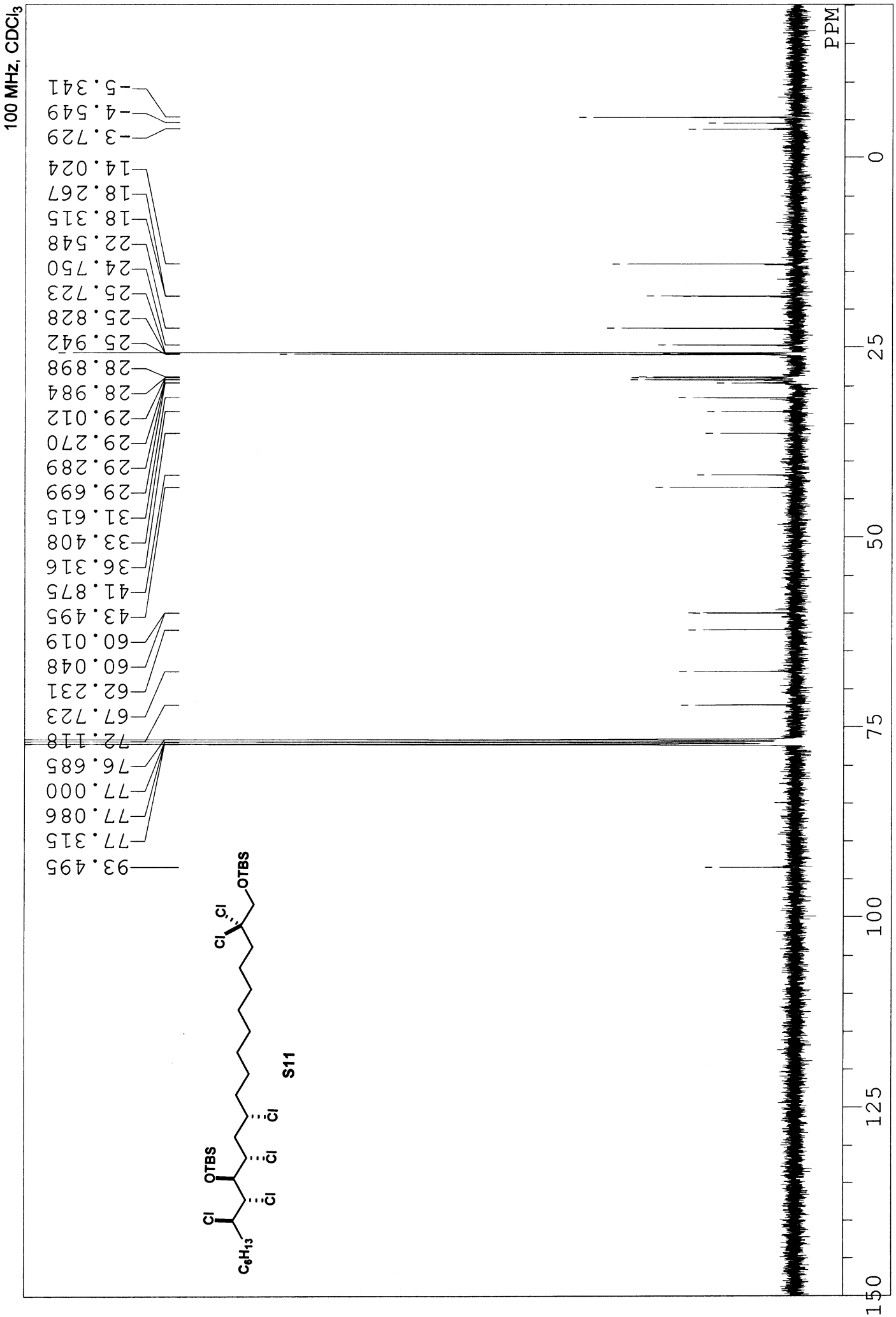
400 MHz, $CDCl_3$

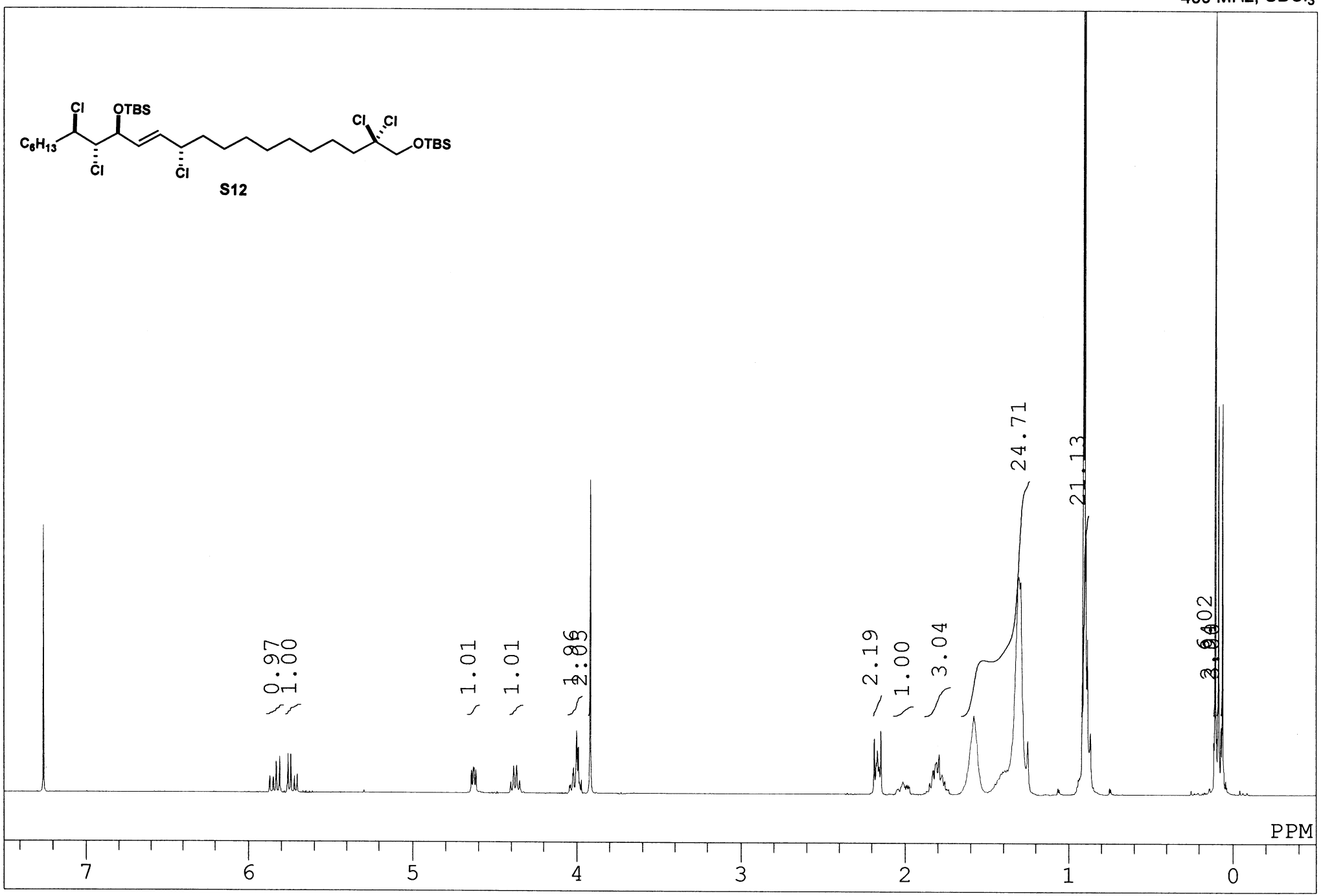


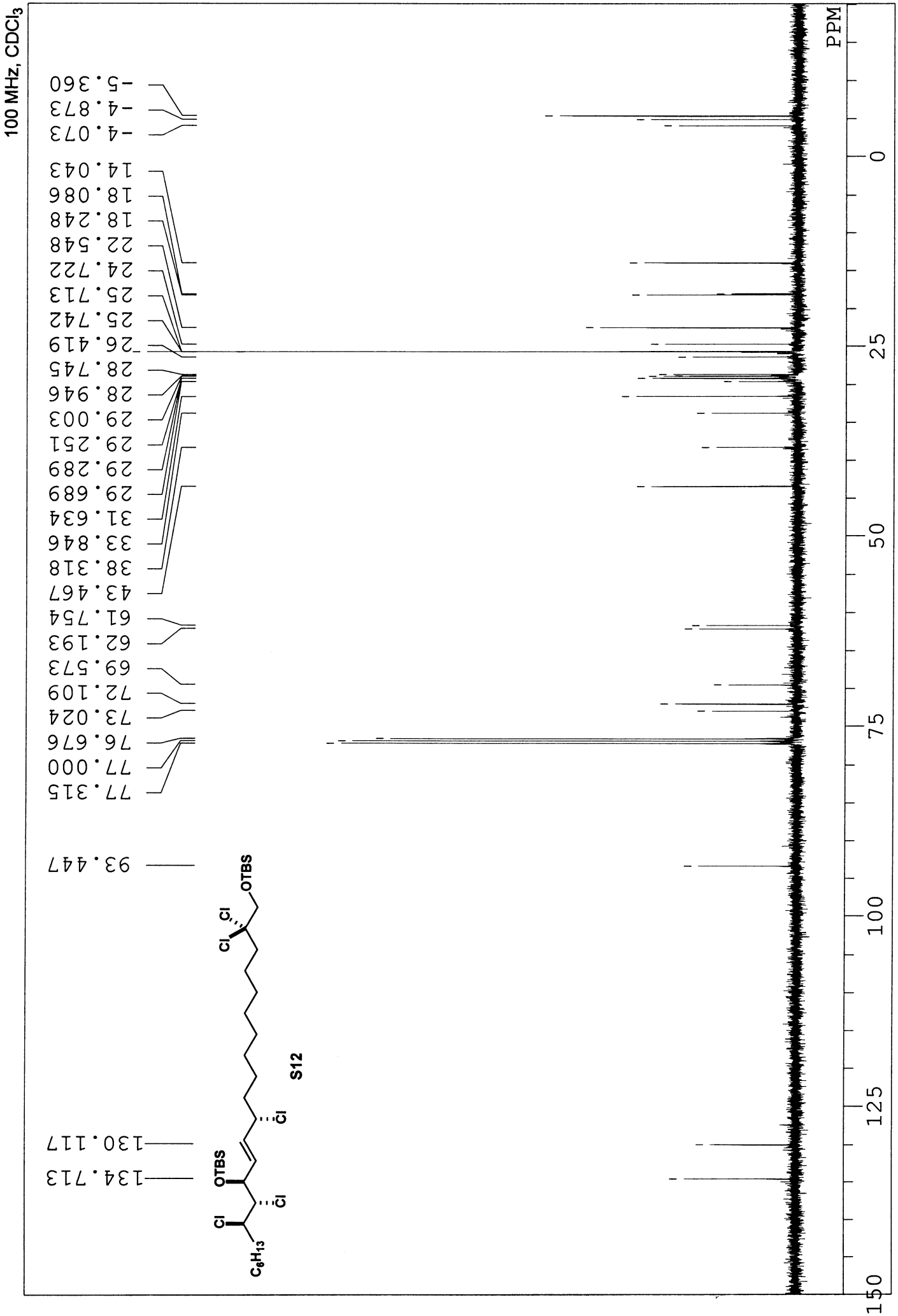
17


100 MHz, CDCl3
-5.350
-3.815
-3.586
14.024
18.248
18.486
22.548
24.712
25.713
25.771
25.952
26.352
26.457
28.965
29.012
29.232
29.251
29.689
31.615
32.769
38.881
43.467
43.896
60.477
61.382
62.021
67.666
72.099
76.590
76.676
77.000
77.315
93.457
PPM
0
25
50
75
100
125
OTBS
Cl
Cl
Cl
Cl
Cl
Cl
Cl
OTBS
C6H13
17

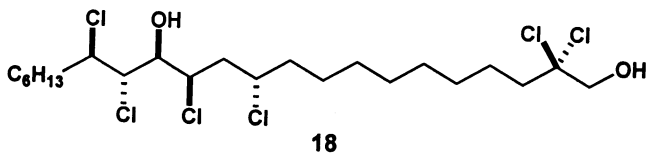

400 MHz, CDCl3
PPM
0
1
2
3
4
5
6
7
2.43
5.00
21.78
34.19
3.06
3.19
1.07
1.92
2.02
1.00
1.96
OTBS
Cl
Cl
Cl
Cl
Cl
OTBS
C6H13
S11


100 MHz, CDCl3
PPM
0
25
50
75
100
125
150
-5.341
-4.549
-3.729
14.024
18.267
18.315
22.548
24.750
25.723
25.828
25.942
28.898
28.984
29.012
29.270
29.289
29.699
31.615
33.408
36.316
41.875
43.495
60.019
60.048
62.231
67.723
72.118
76.685
77.000
77.086
77.315
93.495
OTBS
Cl
Cl
Cl
Cl
Cl
Cl
OTBS
C6H13
S11


400 MHz, CDCl3
Cl
OTBS
C6H13
Cl
Cl
Cl
Cl
OTBS
S12
0.97
1.00
1.01
1.01
2.19
1.00
3.04
24.71
21.13
PPM
7
6
5
4
3
2
1
0

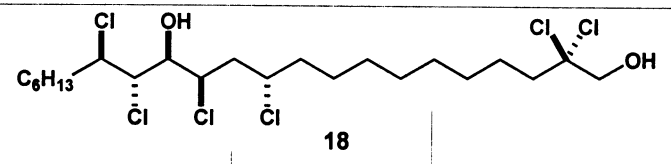

100 MHz, CDCl3
-5.360
-4.873
-4.073
14.043
18.086
18.248
22.548
24.722
25.713
25.742
26.419
28.745
28.946
29.003
29.251
29.289
29.689
31.634
33.846
38.318
43.467
61.754
62.193
69.573
72.109
73.024
76.676
77.000
77.315
93.447
130.117
134.713
OTBS
Cl
Cl
Cl
Cl
Cl
OTBS
C6H13
S12
PPM
0
25
50
75
100
125
150

400 MHz, $CDCl_3$

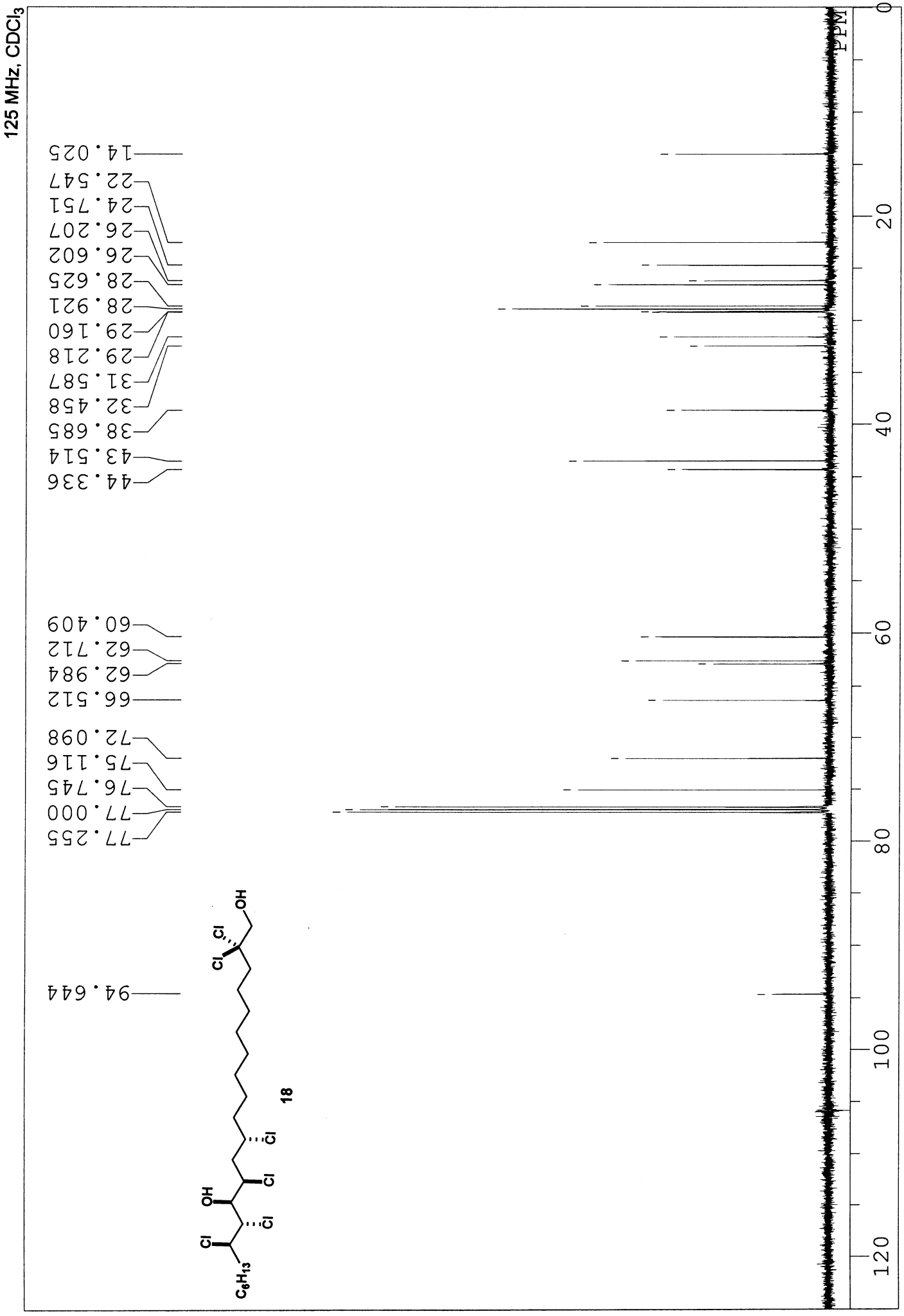


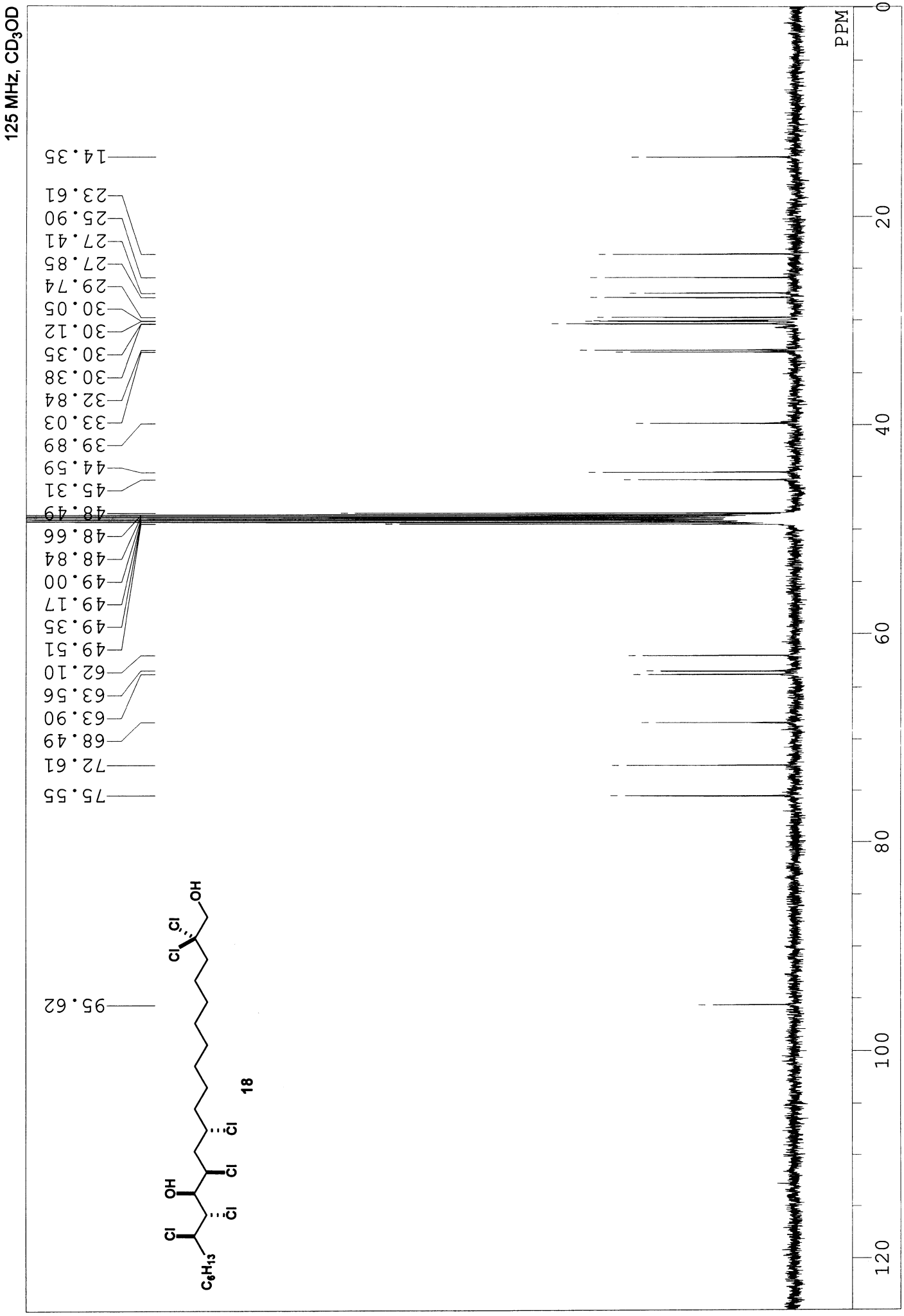
18

400 MHz, CD_3OD

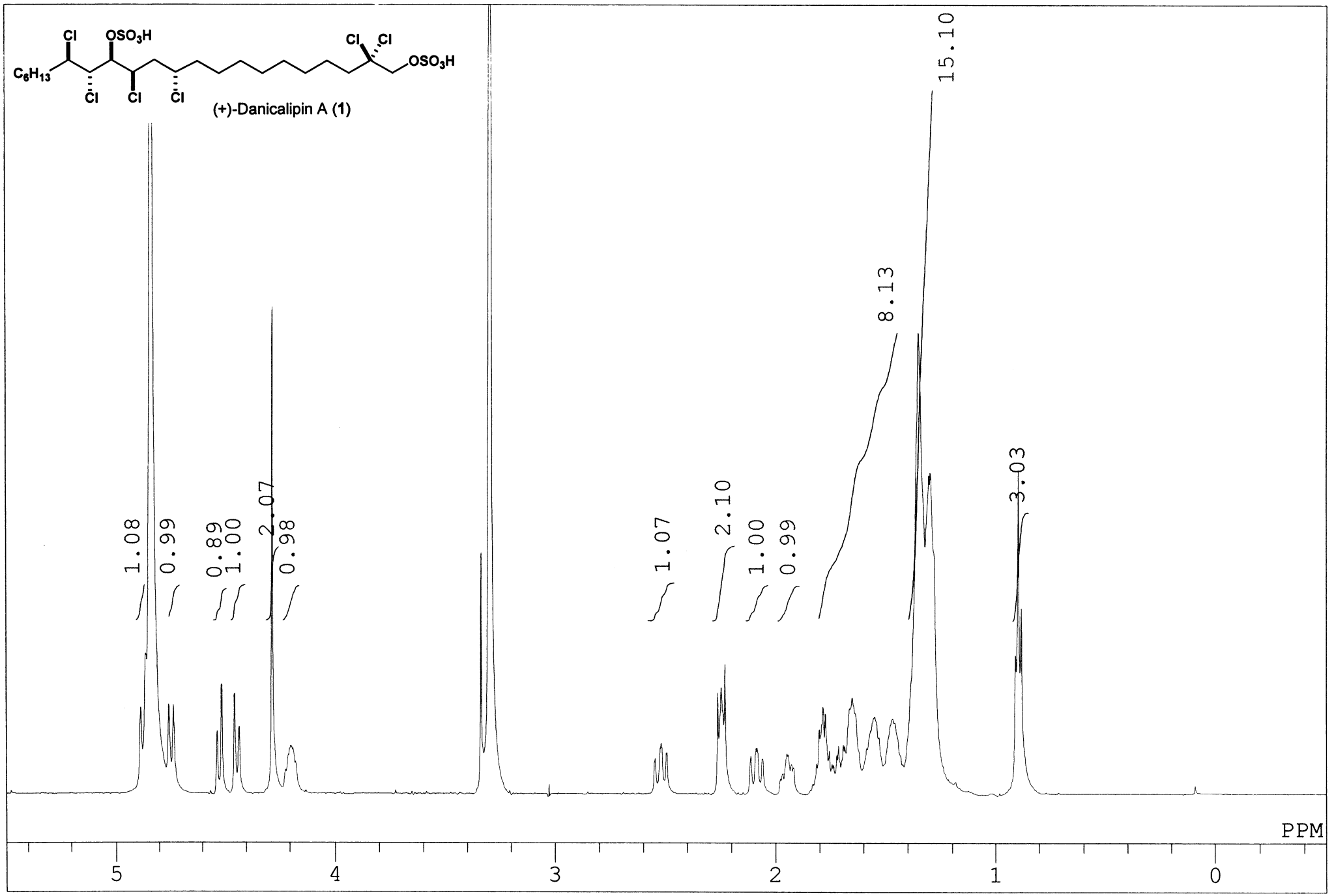


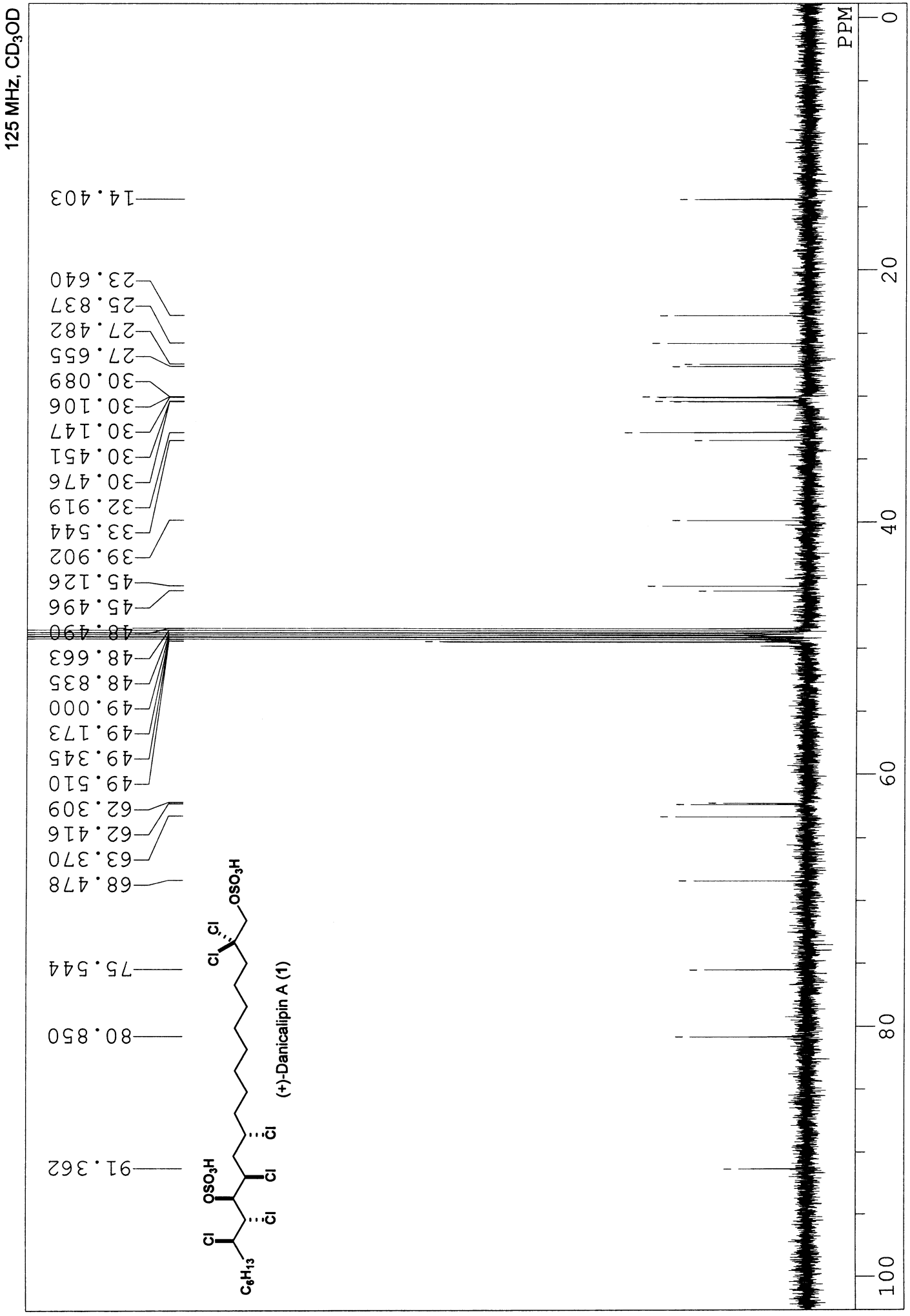
18

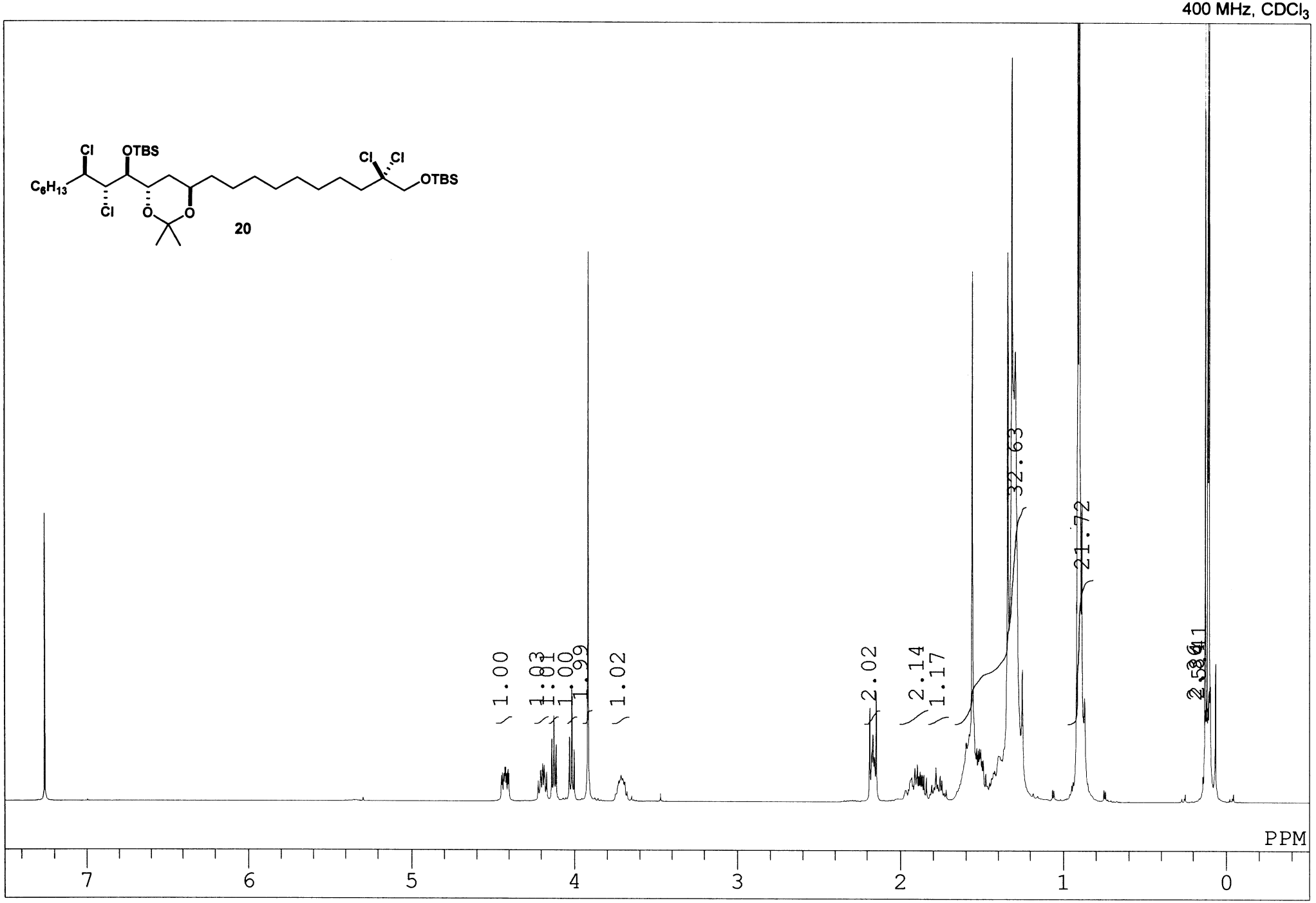

125 MHz, CDCl3
PPM
0
20
40
60
80
100
120
14.025
22.547
24.751
26.207
26.602
28.625
28.921
29.160
29.218
31.587
32.458
38.685
43.514
44.336
60.409
62.712
62.984
66.512
72.098
75.116
76.745
77.000
77.255
94.644
OH
Cl
Cl
Cl
Cl
OH
Cl
Cl
C6H13
18

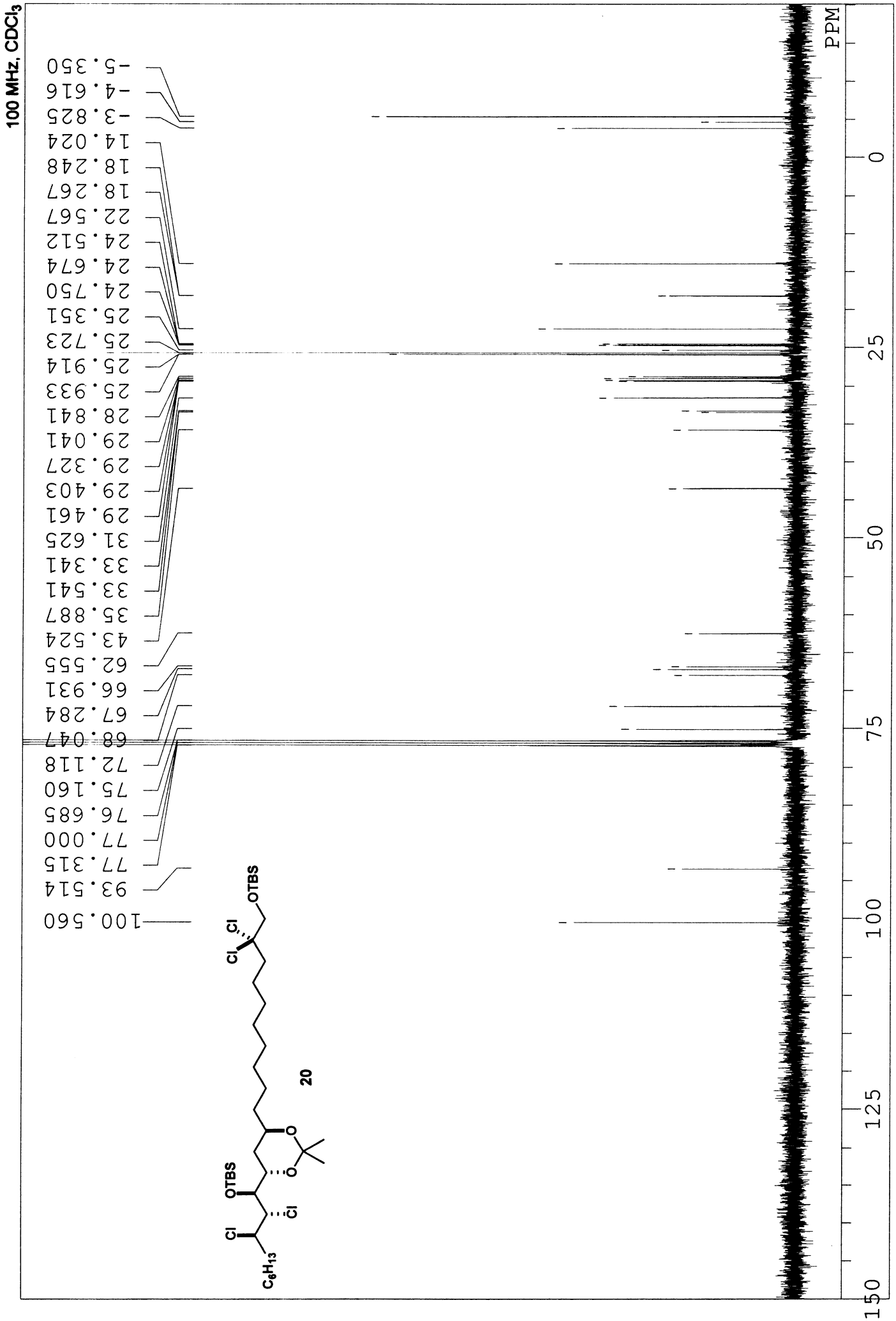

125 MHz, CD3OD
PPM
0
20
40
60
80
100
120
14.35
23.61
25.90
27.41
27.85
29.74
30.05
30.12
30.35
30.38
32.84
33.03
39.89
44.59
45.31
48.49
48.66
48.84
49.00
49.17
49.35
49.51
62.10
63.56
63.90
68.49
72.61
75.55
95.62
OH
Cl
Cl
Cl
Cl
Cl
Cl
OH
Cl
C6H13
18

500 MHz, CD_3OD

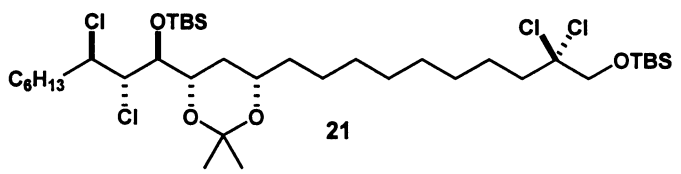



125 MHz, CD3OD
PPM
0
20
40
60
80
100
14.403
23.640
25.837
27.482
27.655
30.089
30.106
30.147
30.451
30.476
32.919
33.544
39.902
45.126
45.496
48.490
48.663
48.835
49.000
49.173
49.345
49.510
62.309
62.416
63.370
68.478
75.544
80.850
91.362
(+)-Danicalipin A (1)
OSO3H
Cl
Cl
Cl
Cl
Cl
Cl
OSO3H
C8H13

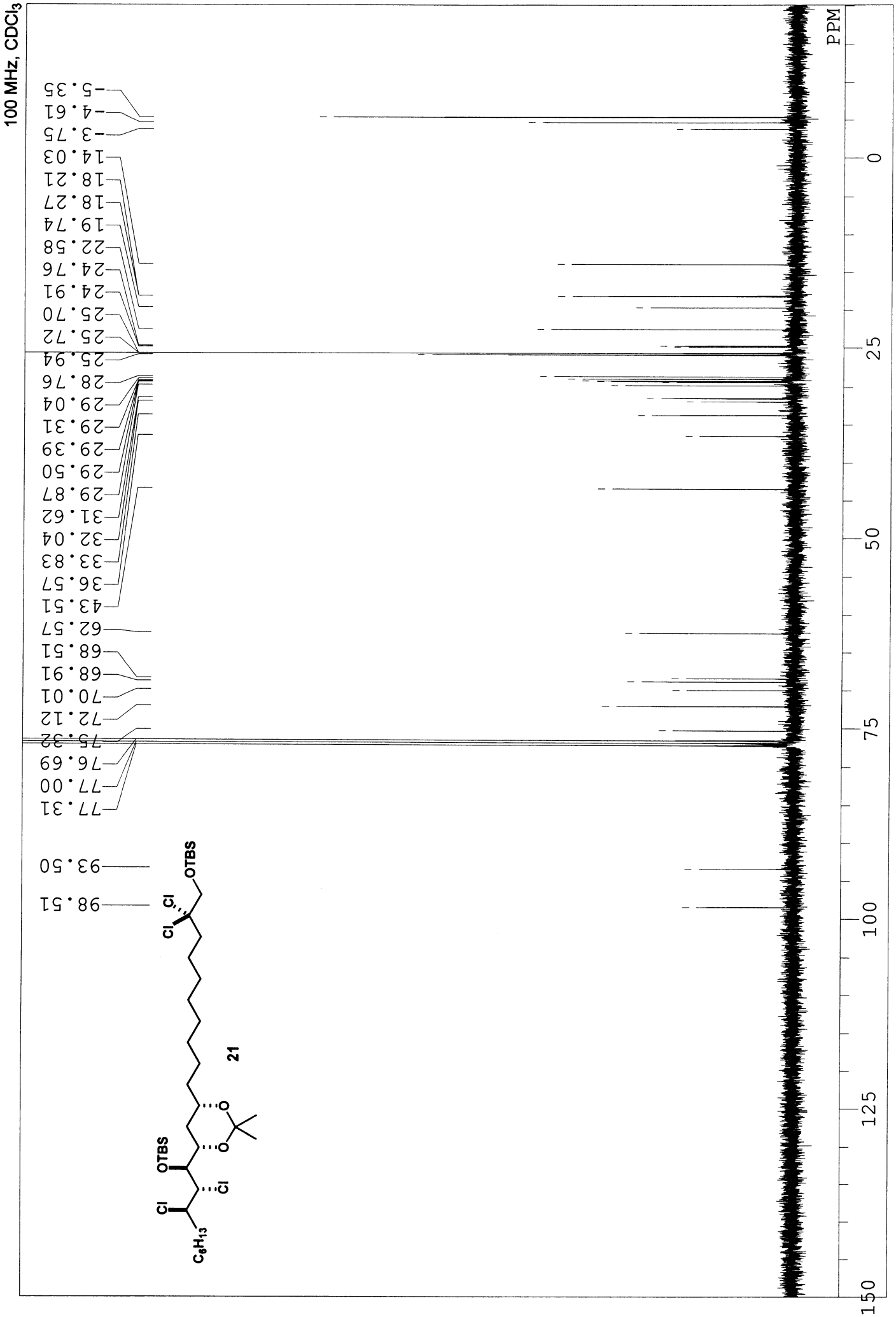

400 MHz, CDCl3
Cl
OTBS
C6H13
Cl
O
O
Cl
Cl
OTBS
20
1.00
1.03
1.01
1.00
1.99
1.02
2.02
2.14
1.17
32.63
21.72
PPM
7
6
5
4
3
2
1
0

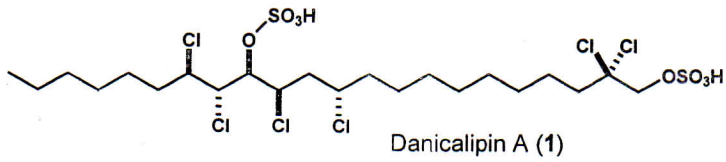

100 MHz, CDCl3
-5.350
-4.616
-3.825
14.024
18.248
18.267
22.567
24.512
24.674
24.750
25.351
25.723
25.914
25.933
28.841
29.041
29.327
29.403
29.461
31.625
33.341
33.541
35.887
43.524
62.555
66.931
67.284
68.047
72.118
75.160
76.685
77.000
77.315
93.514
100.560
PPM
0
25
50
75
100
125
150
OTBS
Cl
Cl
Cl
OTBS
Cl
C6H13
O
O
20

400 MHz, $CDCl_3$



21


100 MHz, CDCl3
PPM
0
25
50
75
100
125
150
-5.35
-4.61
-3.75
14.03
18.21
18.27
19.74
22.58
24.76
24.91
25.70
25.72
25.94
28.76
29.04
29.31
29.39
29.50
29.87
31.62
32.04
33.83
36.57
43.51
62.57
68.51
68.91
70.01
72.12
75.32
76.69
77.00
77.31
93.50
98.51
OTBS
Cl
Cl
OTBS
Cl
Cl
C6H13
21



Danicalipin A (**1**)

synthetic

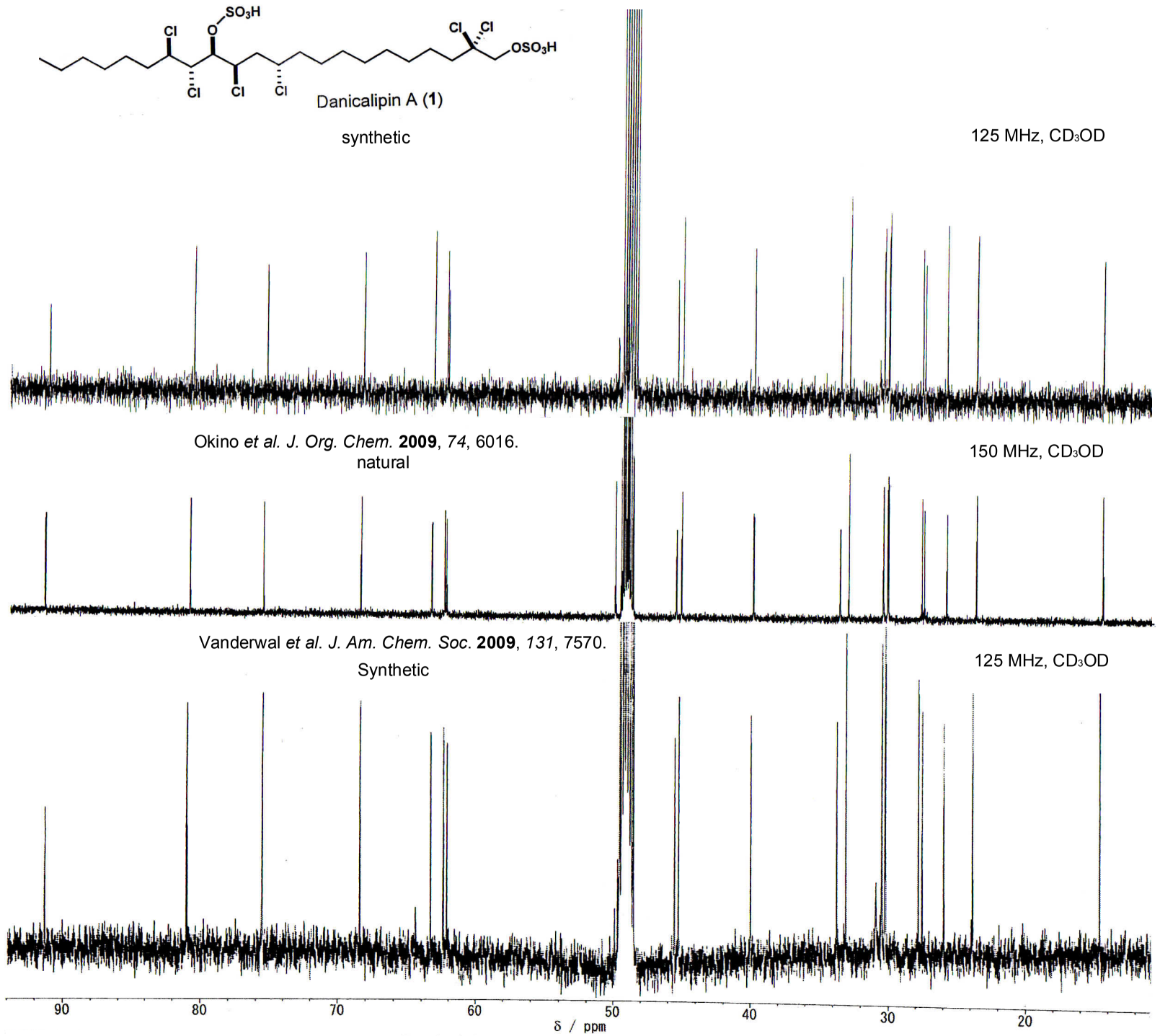
500 MHz, CD_3OD

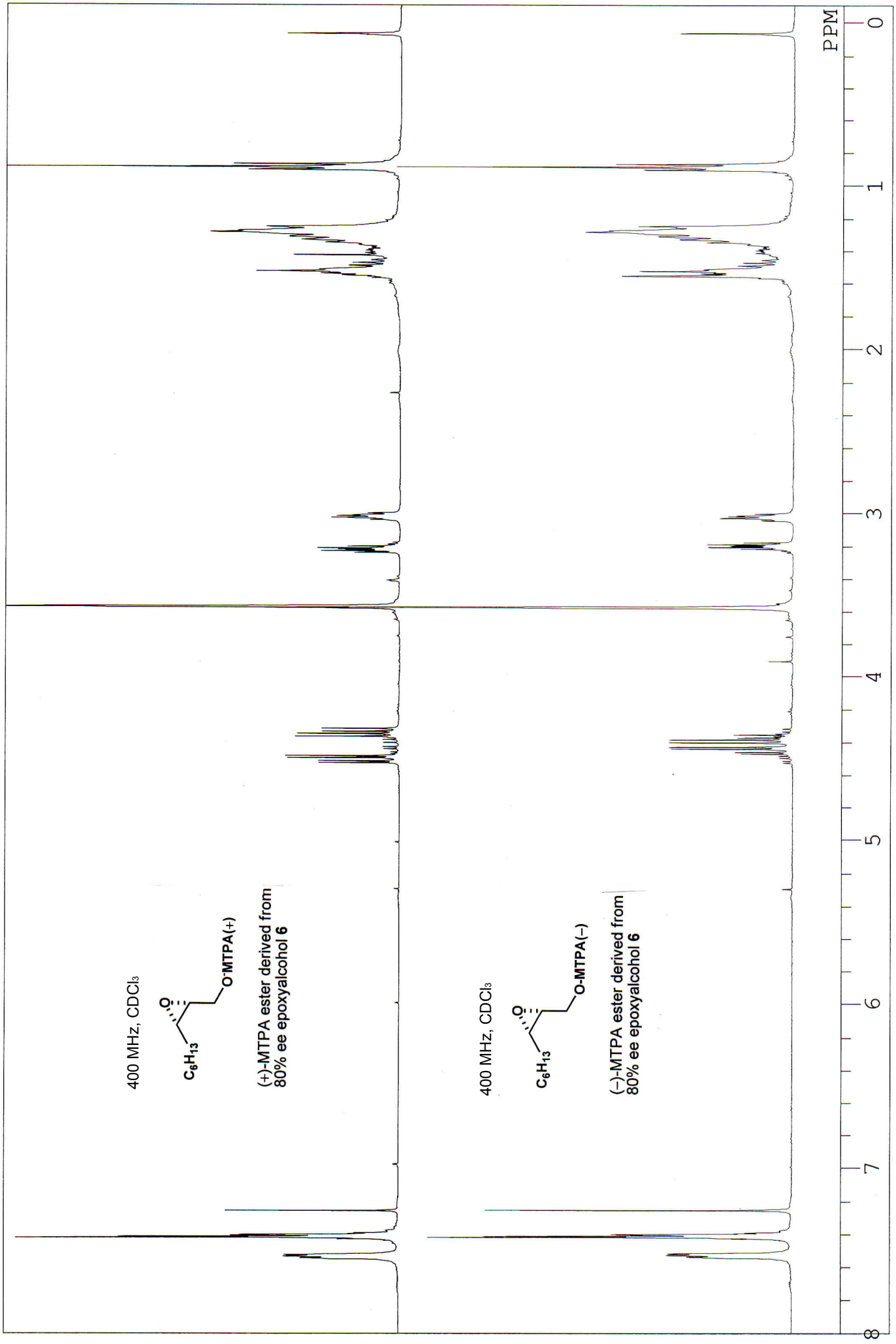
600 MHz, CD_3OD

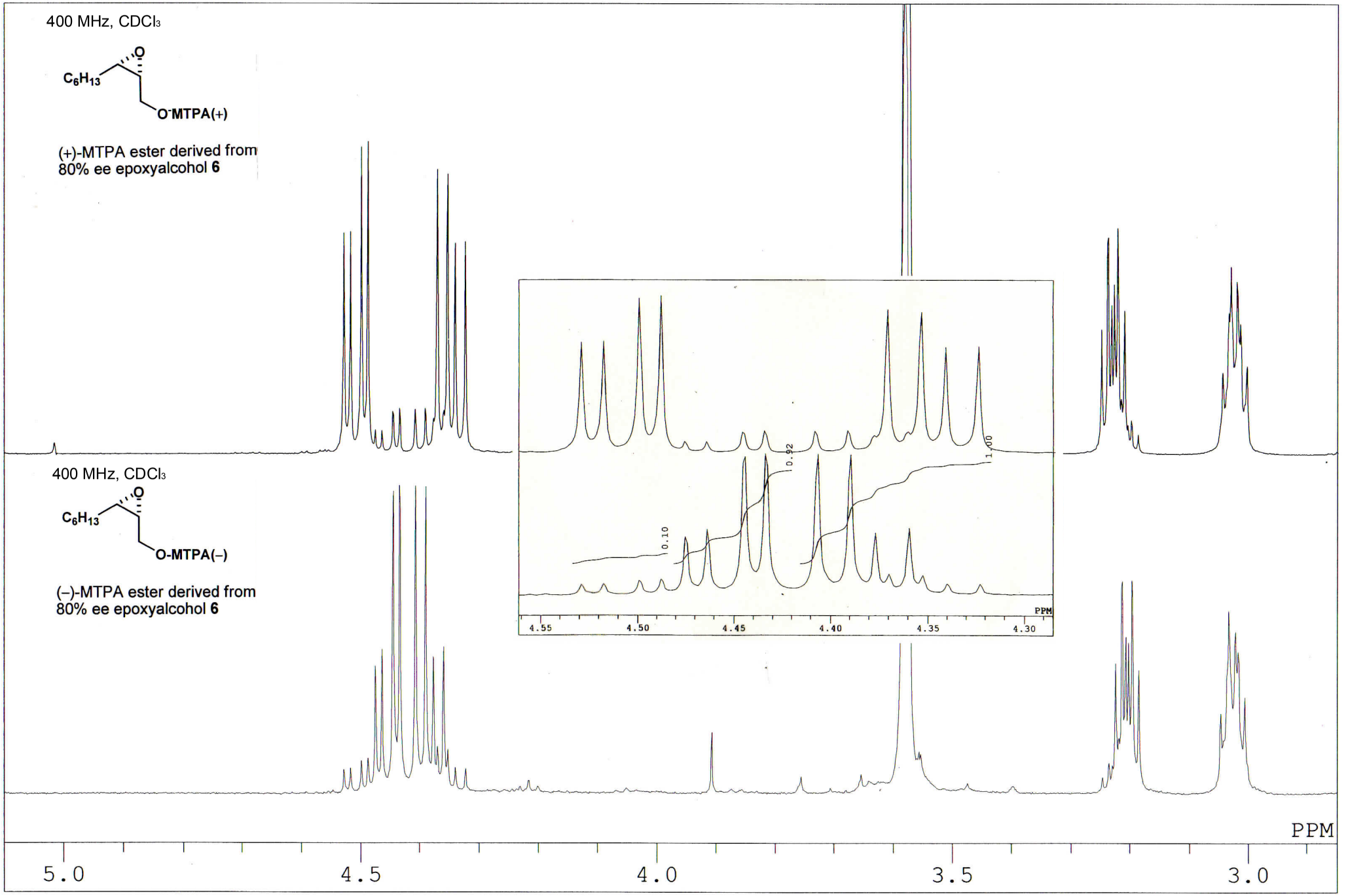
Okino *et al. J. Org. Chem.* **2009**, *74*, 6016.

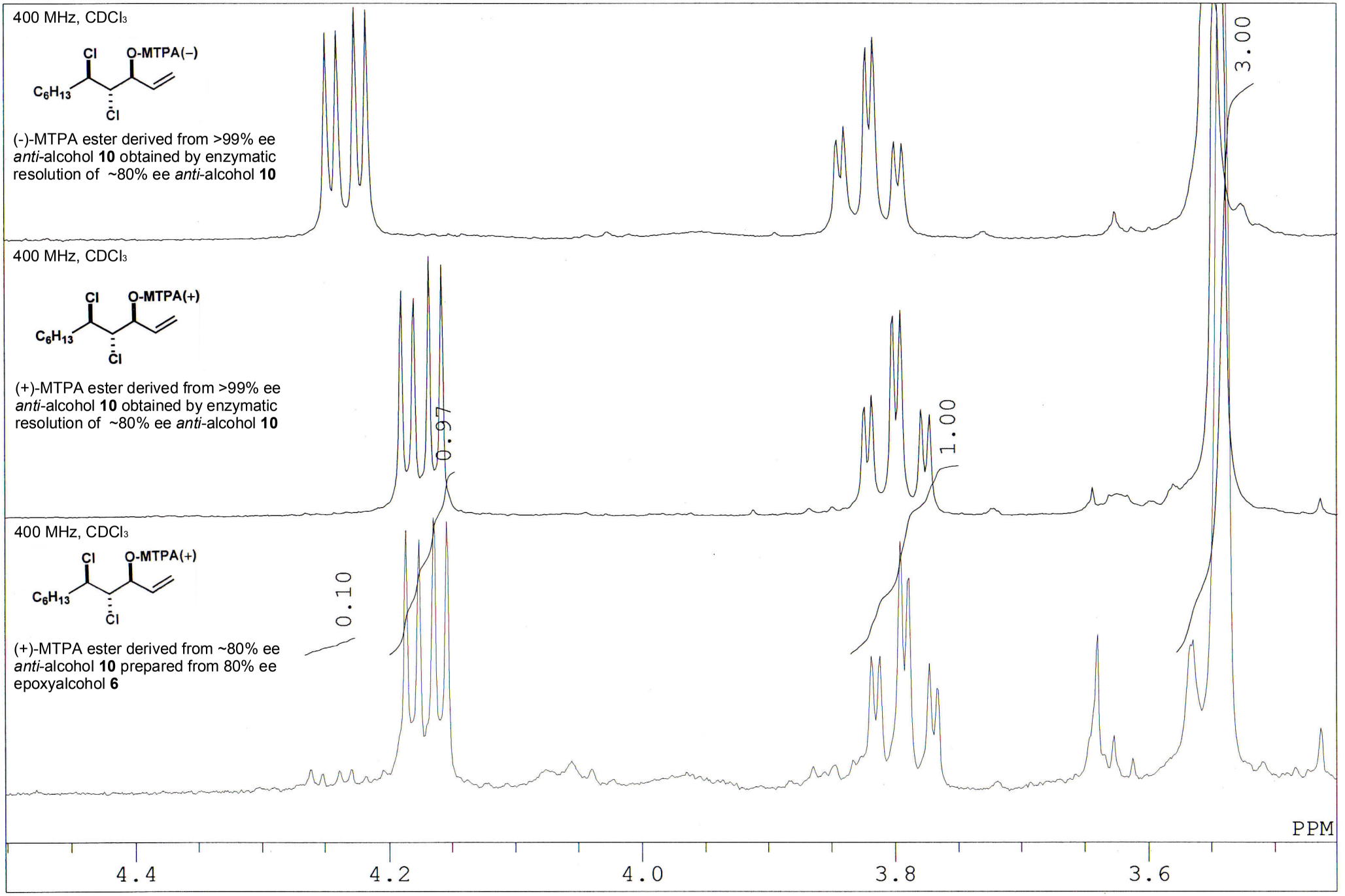
500 MHz, CD_3OD

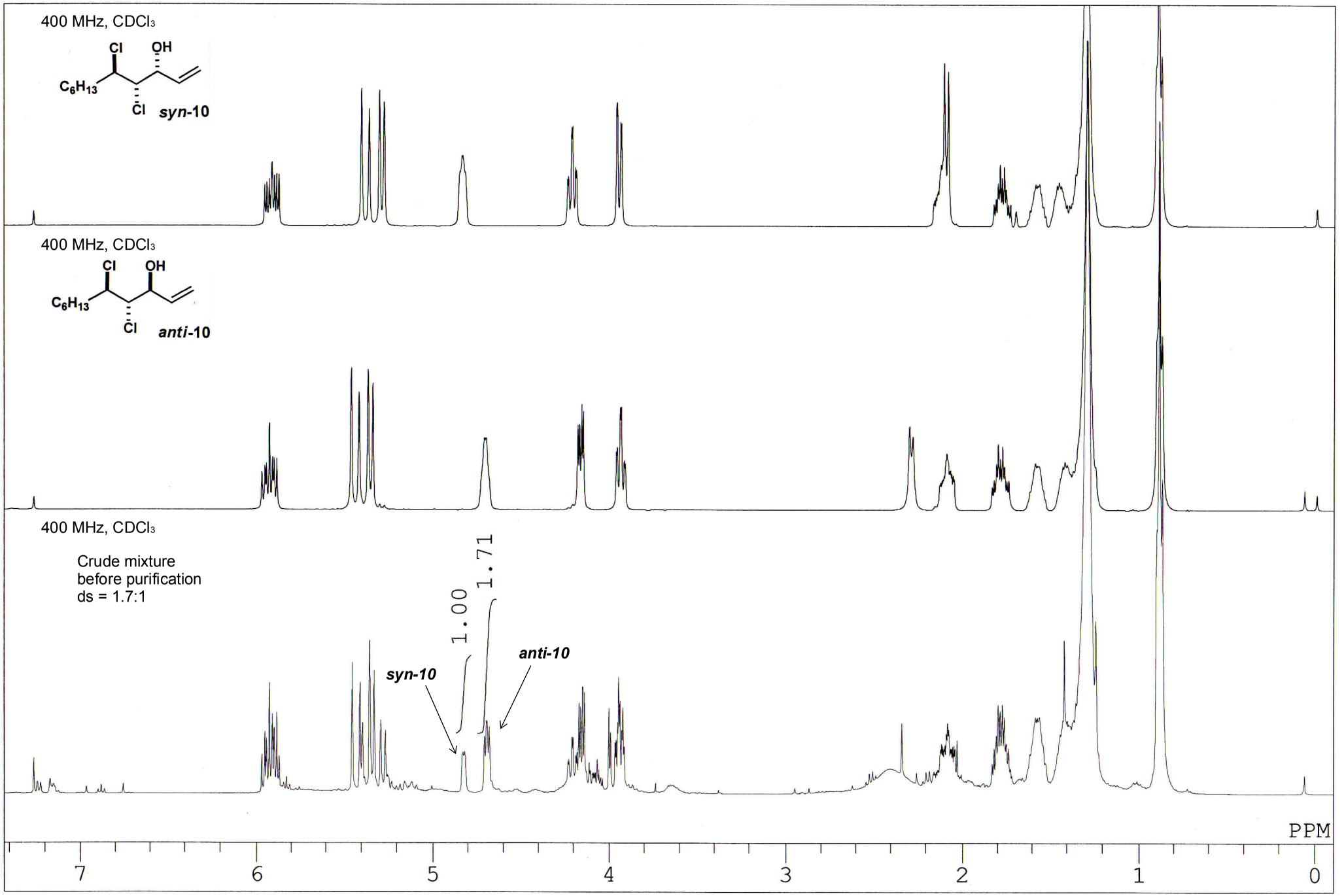
Vanderwal *et al. J. Am. Chem. Soc.* **2009**, *131*, 7570.

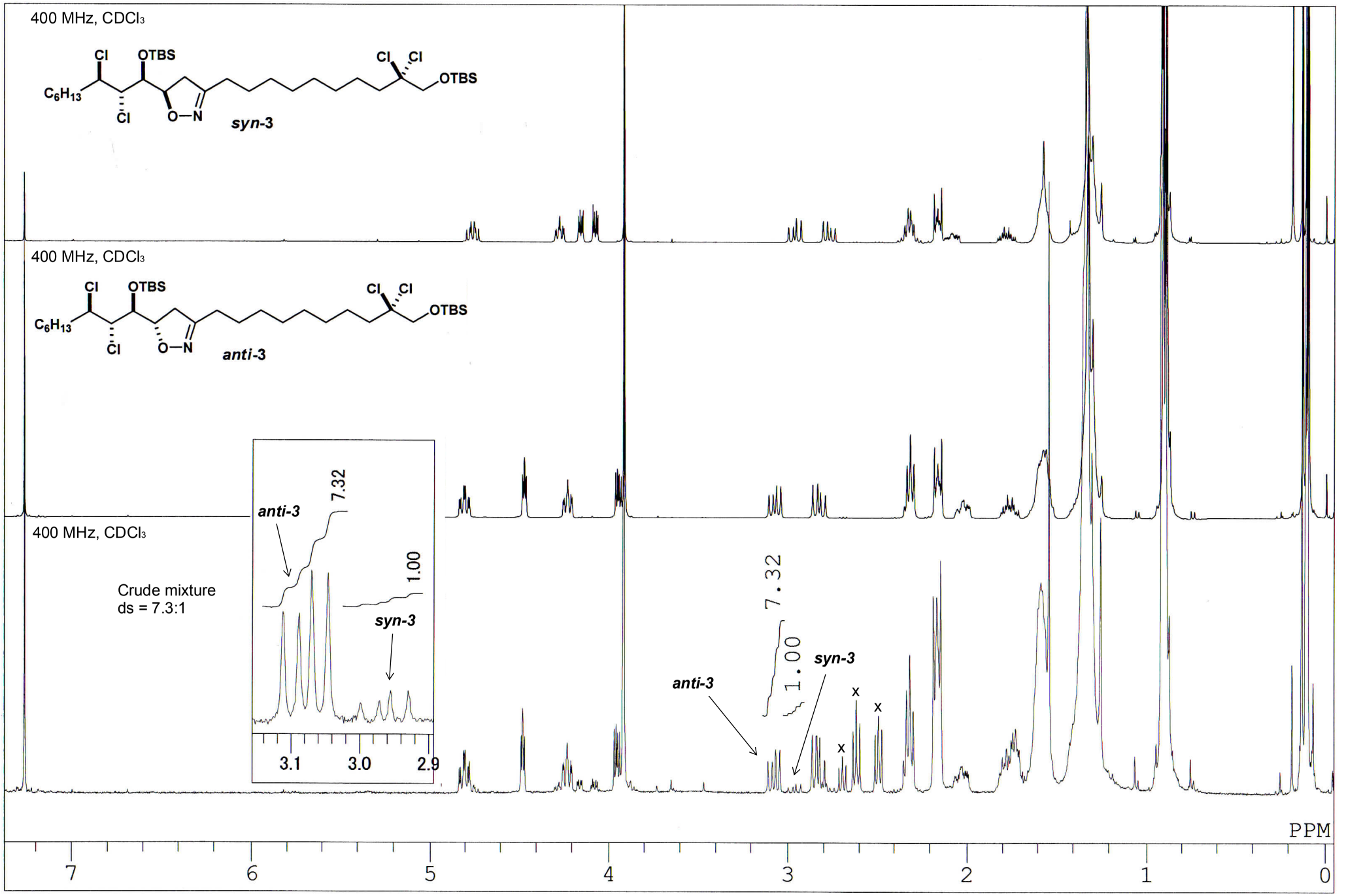

SO3H
Cl
O
Cl
Cl
Cl
Cl
Cl
OSO3H
Danicalipin A (1)
synthetic
125 MHz, CD3OD
Okino et al. J. Org. Chem. 2009, 74, 6016.
natural
150 MHz, CD3OD
Vanderwal et al. J. Am. Chem. Soc. 2009, 131, 7570.
Synthetic
125 MHz, CD3OD
90
80
70
60
50
40
30
20
δ / ppm

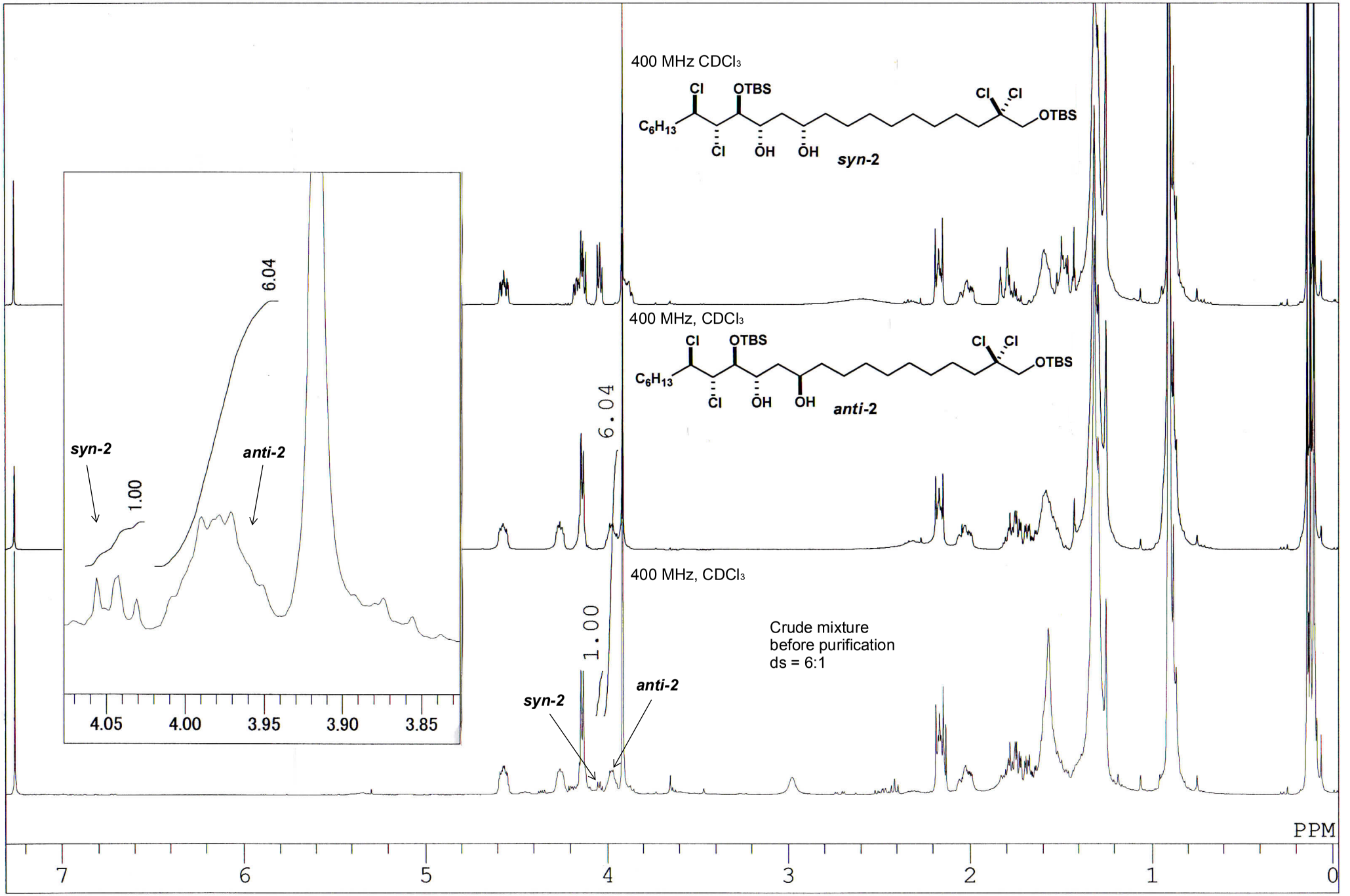

400 MHz, CDCl3
C6H13
O-MTPA(+)
(+)-MTPA ester derived from
80% ee epoxyalcohol 6
400 MHz, CDCl3
C6H13
O-MTPA(–)
(–)-MTPA ester derived from
80% ee epoxyalcohol 6
PPM
0
1
2
3
4
5
6
7
8


400 MHz, CDCl3
C6H13
O-MTPA(+)
(+)-MTPA ester derived from
80% ee epoxyalcohol 6
400 MHz, CDCl3
C6H13
O-MTPA(–)
(–)-MTPA ester derived from
80% ee epoxyalcohol 6
0.10
0.92
1.00
4.55
4.50
4.45
4.40
4.35
4.30
PPM
5.0
4.5
4.0
3.5
3.0
PPM


400 MHz, CDCl3
Cl
O-MTPA(–)
C6H13
Cl
(-)-MTPA ester derived from >99% ee anti-alcohol 10 obtained by enzymatic resolution of ~80% ee anti-alcohol 10
3.00
400 MHz, CDCl3
Cl
O-MTPA(+)
C6H13
Cl
(+)-MTPA ester derived from >99% ee anti-alcohol 10 obtained by enzymatic resolution of ~80% ee anti-alcohol 10
0.97
1.00
400 MHz, CDCl3
Cl
O-MTPA(+)
C6H13
Cl
(+)-MTPA ester derived from ~80% ee anti-alcohol 10 prepared from 80% ee epoxyalcohol 6
0.10
PPM
4.4
4.2
4.0
3.8
3.6


400 MHz, CDCl3
Cl
OH
C6H13
Cl
syn-10
400 MHz, CDCl3
Cl
OH
C6H13
Cl
anti-10
400 MHz, CDCl3
Crude mixture
before purification
ds = 1.7:1
1.00
1.71
syn-10
anti-10
PPM
7
6
5
4
3
2
1
0


400 MHz, CDCl3
Cl
OTBS
Cl
Cl
C6H13
Cl
O—N
OTBS
syn-3
400 MHz, CDCl3
anti-3
400 MHz, CDCl3
Crude mixture
ds = 7.3:1
anti-3
7.32
syn-3
1.00
3.1
3.0
2.9
7.32
1.00
anti-3
syn-3
x
x
x
PPM
7
6
5
4
3
2
1
0


400 MHz CDCl3
Cl
OTBS
Cl
Cl
C6H13
Cl
OH
OH
OTBS
syn-2
400 MHz, CDCl3
anti-2
6.04
1.00
syn-2
anti-2
400 MHz, CDCl3
Crude mixture
before purification
ds = 6:1
4.05
4.00
3.95
3.90
3.85
PPM
7
6
5
4
3
2
1
0